Effectiveness of Aerosol Filtration by Mechanical Filter, Electrostatic Filter, and Electrostatic Filter with Heat Moisture Exchanger in Healthy Volunteers Nebulized with Normal Saline: A Randomized Crossover Trial

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Background: The COVID-19 outbreak in Thailand has raised concerns that aerosol generated from the nebulizer might be contaminated with SARS-CoV-2. To prevent this, various types of viral filters might be useful in decreasing the spread of COVID-19.

Objective: To compare the effectiveness of mechanical filter, electrostatic filter, and electrostatic filter with heat moisture exchanger (HME) to no filter in filtration nebulized normal saline solution (NSS).

Materials and Methods: The present study was a randomized, single-blind crossover trial. Forty-eight healthy volunteers were given nebulized NSS via the mouthpiece. At the end of the system, a filter or no filter was attached according to the randomization series. The primary outcome was the number of particles per cubic foot measured at two locations, distal to the filter, which is referred to as 'near distant' and 180 centimeters away from the system, which is referred to as 'far distant' during nebulization. The measurement was recorded every minute from the beginning of nebulization until the fifth minute.

Results: Forty-eight healthy volunteers were studied with four types of filtration methods. The number of particles per cubic foot was compared by intervention using a multi-level mixed effect linear regression, a statistical method that accounted for the repeated measurements within each participant. The highest number of particles was measured at the near distant in no filter group, with a mean of 188,034 particles per cubic feet and a maximum of 370,816 particles per cubic feet and lowest number was measured at the far distant in mechanical filter group with a mean of 199 per cubic feet and a maximum of 316 particles per cubic feet. The ranking of the number of particles from the highest to the lowest were no filter, electrostatic filter, electrostatic filter with HME, and mechanical filter. Each type of filter significantly decreased the number of particles compared to no filter usage ($p<0.001$). However, no significant difference was found among each type of filter.

Conclusion: Mechanical filter, electrostatic filter, and electrostatic with HME lessened the number of particle dispersion into the environment compared with no filter attached to the nebulization equipment.

Keywords: Aerosol filtration; Nebulized; Mechanical filter; Electrostatic filter; Electrostatic filter HME; Filter

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The COVID-19 outbreak in Thailand has raised concerns that aerosols generated from nebulizers might contaminate with SARS-CoV-2(1,2). In many emergency departments, there may not be designated areas for nebulization that prevent aerosol dispersion. Metered-dose inhaler techniques may decrease aerosol spreading compared to nebulization, but they might be inadequate for some groups of patients, especially the elderly(3). Therefore, nebulization remains essential despite generating aerosols in some populations(4).

A respiratory system filter is required to prevent the spread of COVID-19 or other airborne particles during nebulization. There are two types of filters available. The first type is a mechanical filter, which operates by the mechanical properties of airflow, fibers, and particles. Large particles are filtrated by interception and inertia, while small particles are filtrated by diffusion(5). Mechanical filters require a large filtration area to work effectively. The second

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type is an electrostatic filter, where an electrostatic charge is added to the filter's fibers, attracting and capturing particles with the opposite charge(6). This type of filter is smaller, and its fibers are looser, causing less pressure drop across the filter than mechanical filters(7). However, electrostatic filters are hydrophobic, whereas mechanical filters are hydrophilic. As a result, aerosols are more likely to penetrate electrostatic filters than mechanical filters. Nevertheless, water droplets retained by the dense fibers of hydrophilic mechanical filters may cause more resistance than electrostatic filters. Another property that can be added to filters is the heat moisture exchanger (HME) function. The HME part of the filters retains heat and moisture in the exhaled air at the filters and returns it to the inhaled air. Filters with this property might be able to filter more water droplets but cause more resistance compared to filters without this property.

The present study aimed to compare the effectiveness of filtration of aerosols by three filters, mechanical filter, electrostatic filter, and electrostatic filter with HME, as well as the resistance across filters after normal saline nebulization administered to healthy volunteers. The authors hypothesized that a mechanical filter might be the most effective in reducing the dispersion of nebulized normal saline solution (NSS) particles into the environment compared to other filters.

In the present study, the authors used AEROTRAK™ handheld airborne particle counter model 9306 to measure the number of particles contaminated in the environment. This equipment can measure particles between 0.3 to 25 µm size range, while the SARS-CoV-2 has been reported to be found in particle sizes more than 0.34 µm and most of the virus is found in particles less than 4.5 µm(8).

Materials and Methods

The present study protocol was approved by the Human Research Ethics Committee, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, on May 31, 2022 (COA. MURA2022/314). It was registered at thaiclinicaltrials.org (study ID TCTR20220729002). The present study was conducted at Ramathibodi Hospital, Thailand, between December 1, 2022 and February 28, 2023. The trial was conducted in accordance with the principles stated in the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from all volunteers before participating in the study.

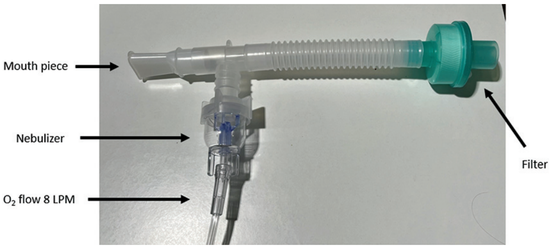

Figure 1. Assembly of small volume nebulizer connected with mouthpiece, reservoir tube, and electrostatic filter with HME.

Study design and participants

The present study was designed as a randomized, single-blind crossover trial. Healthy volunteers between 20 and 65 years of age were included. Participants with a history of recent or current respiratory symptoms, chronic respiratory diseases, asthma, cardiovascular disease including cardiomegaly and congestive heart failure, pregnancy, or normal saline allergies were excluded. All participants were nebulized with normal saline four times, with different types of filters or no filter attached each time in different sequences.

Randomization and masking

Subjects were randomized into 24 sequences according to the order of filtration methods. Three types of filters were tested, Covidien DAR™ mechanical filter, Covidien DAR™ electrostatic filter, and Covidien DAR™ electrostatic filter with HME. Nebulization without filter was used as a control group. Simple randomization was generated using the online software (www.sealedenvelope.org) by the research assistant. Allocation sequences were concealed using a closed envelope method. The envelope was opened after a blindfold was applied to the participant. CB enrolled and assigned the participants to interventions.

Intervention

Baseline room particle concentration was measured by an AEROTRAK™ handheld airborne particle counter model 9306 before normal saline nebulization and recorded as the amount per cubic foot. Five milliliters of normal saline was delivered by a small-volume nebulizer connected to a mouthpiece, reservoir tube, and filter. The filter was attached at the end of the reservoir tube, as shown in Figure 1. The oxygen flow meter was set at a rate of 8 liters per minute during nebulization. Nebulization lasted five minutes. The number of particles per cubic foot during nebulization was measured each minute for five minutes at near or just distal to the filter, and far or 180 centimeters away from the nebulization system, distances.

After five minutes, the used filter was attached to a Y-piece in an anesthetic machine (Avance™ CS² Anesthesia Delivery System) connected to a test lung and ventilated with volume-controlled ventilation with a tidal volume of 500 mL, respiratory rate of 10 breaths per minute, and an I to E ratio of 1:5. Airway pressure (cmH_2O) was measured by a pressure transducer attached proximal and distal to the used filter. The number was continuously displayed on a monitor screen. The maximum number was recorded by an investigator. A 10-minute break was provided as a particle washout period for each method. The baseline room particle concentration was checked before performing nebulization with the next filtration method. The next nebulization was started after the baseline room particle concentration returned to baseline or within 10% of the baseline level.

Outcomes

The primary outcome was the number of particles per cubic foot. The data were compared between each type of filter and no filter at near and far distances by using maximum and mean particles per cubic foot. The secondary outcome was airway pressure across each type of filter.

Statistical analysis

The sample size was calculated using a multiple-sample Williams crossover trial design, thus, a 4 by 4 crossover. The Harnois et al. study compared the nebulization system with a filter to the system without a filter and found that adding a filter to the system decreased particle output by around 50%(9). However, no previous study has compared each type of filter. Therefore, we chose a 10% difference to calculate the number of populations in this study since the authors believe that would have a clinical significance. A sample size of 48 subjects was needed to have 80% power to detect the minimal detectable differences of 10% among the filter groups.

Data were described using mean and standard deviation (SD), median, and range as appropriate for continuous variables and percentage for categorical variables. The primary outcome was compared between mechanical filter, electrostatic filter, electrostatic with HME filter, and no filter groups with repeated measures using multilevel mixed-effects linear regression, presented by mean difference and 95% confidence interval (CI). Statistical analyses were performed using Stata Statistical Software, version 17 (StataCorp LLC, College Station, TX, USA), with a significant threshold p-value of less than 0.05 (2-sided).

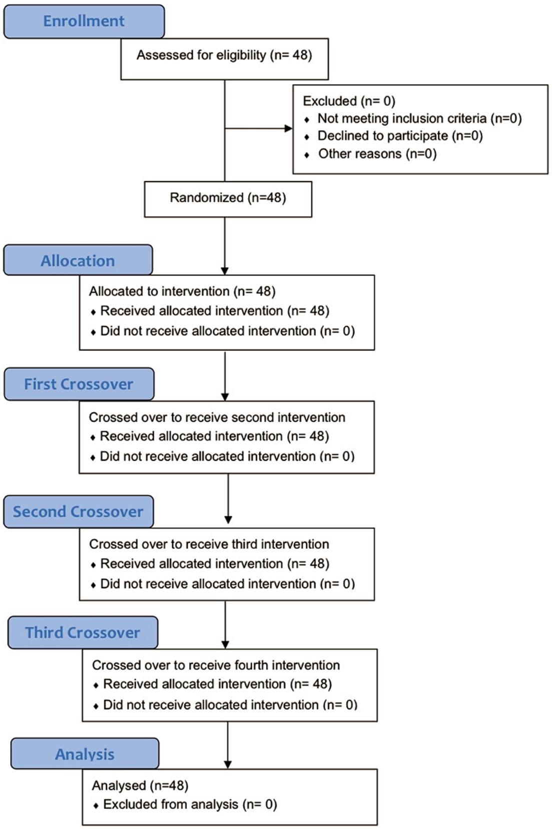

Figure 2. CONSORT flow diagram illustrating volunteer enrollment through analysis.

Table 1. Demographic data

Characteristics	n=48
Age (year); mean [SD]	36.7 [10.8]
Sex; n (%)	
Female	21 (43.8)
Male	27 (56.2)
Weight (kg); mean [SD]	63.7 [11.7]
Height (cm); mean [SD]	166.3 [9.4]
BMI (kg/m^2); mean [SD]	22.9 [3.0]

SD=standard deviation; BMI=body mass index

Results

Forty-eight participants were enrolled. All volunteers received the intervention, and all data were analyzed. The CONSORT flow diagram is shown in Figure 2. Demographic data of participants are shown in Table 1. Fifty-six percent of participants were male,

Table 2. Each filtration method's average and maximum number of particles at near and far distances

Distant	Intervention	Average particle; mean (SE)	Maximum particle; mean (SE)
Near	Mechanical filter	1,964.12 (16,497.26)	3,963.52 (48,889.87)
	Electrostatic filter	2,664.83 (16,497.26)	5,440.60 (48,889.87)
	Electrostatic filter with HME	2,220.46 (16,497.26)	3,820.92 (48,889.87)
	No filter	188,034.00 (16,497.26)	370,816.00 (48,889.87)
Far	Mechanical filter	199.19 (54.61)	316.85 (151.33)
	Electrostatic filter	278.74 (54.61)	480.35 (151.33)
	Electrostatic filter with HME	215.53 (54.61)	319.15 (151.33)
	No filter	958.22 (54.61)	1,605.40 (151.33)

SE=standard error; HME=heat moisture exchanger

Table 3. The maximum number of particles compared between interventions

Intervention	MD (95% CI)	p-value
Mechanical filter vs. no filter	–184,070.50 (–256,686.70 to –111,454.40)	<0.001
Electrostatic filer vs. no filter	–183,250.20 (–255,866.40 to –110,634.10)	<0.001
Electrostatic filter with HME vs. no filter	–184,140.70 (–256,756.80 to –111,524.60)	<0.001
Electrostatic filter vs. mechanical filter	820.3 (–71,795.80 to 73,436.40)	0.982
Electrostatic filter with HME vs. mechanical filter	–70.2 (–72,686.30 to 72,546.0)	0.998
Electrostatic filter with HME vs. electrostatic filter	–890.4 (–73,506.60 to 71,725.70)	0.981

MD=mean difference; CI=confident interval; HME=heat moisture exchanger

with an average age of 36.7 years.

Table 2 presents each filtration method's average and maximum number of particles at near and far distances. The number of particles measured at near distances ranked from highest to lowest were no filter at 188,034, electrostatic filter at 2,664.83, electrostatic filter with HME at 2,220.46, and mechanical filter at 1,964.12. The average and maximum number of particles measured at far distances similarly showed the same sequences as mean particles measured at near distances. However, the ordering of the maximum number of particles counted at near distances showed different results. The maximum number of particles was highest in the no filter group with 370,816, followed by the electrostatic filter with 5,440.6, mechanical filter with 3,963.52, and electrostatic filter with HME group with 3,820.92.

The effectiveness of filtration by each type of filter is revealed in Table 3. All three types of filters significantly lowered the number of particles compared to no filter. There was no statistically significant difference in the maximum number of particles among each type of filter.

The mean pressure across the filter was 0.1 cmH_2O for the mechanical filter, 0.1 cmH_2O for the electrostatic filter, and 0.25 cmH_2O for the electrostatic filter with HME. There was no statistically significant difference in airway pressure across the filters among groups.

Discussion

The present study shows that mechanical, electrostatic, and electrostatic filters with HME effectively decrease particle dispersions into the environment. However, none of the filters demonstrated superiority in the filtration of NSS aerosols compared to the other filters. This contradicts the previous studies that indicated exposure to moisture can reduce the effectiveness of electrostatic filters, leading to deterioration over time(10,11). Several factors may account for this discrepancy. First, the brief period of nebulization in the present study might be inadequate to reveal the deterioration of the filter function. In the present study, the nebulization was performed only once for five minutes. In previous studies, electrostatic filters were exposed to high humidity for 48 hours or even one week to demonstrate filter dysfunction(10,11). Moreover, filters with HME function were reported to reach their humidification efficiency after 10 to 30 minutes, depending on the material types, which suggests that it may take 10 to 30 minutes before the HME is saturated with humidity(6). Therefore, in the present study, any filter effectively decreases particle dispersion into the environment, but increasing time or repeating doses of nebulization might affect the efficacy in filters. The second reason that might explain the effectiveness of all filter types was not different is the amount of NSS used. A higher amount of NSS may be required to affect filter permeability. The present study used 5 mL of NSS to mimic emergency department nebulization, but the filter can contain a volume up to 20 to 25 mL(12). In Turnbull et al.'s study, NSS was added directly to the filter compared to the present study, where healthy volunteers inhaled 5 mL of NSS before breathing out through the filter during exhalation(12). This causes even lower amounts of volume to accumulate in the filter. In summary, a brief period of nebulization and the low amount of NSS used in the present study are the possible reasons that cause no difference between the types of filters.

The secondary objective of the present study was to investigate the discrepancy in pressure across filters among various filter types. Prior studies have demonstrated that following exposure to aerosols or humidity, there is an increase in respiratory system resistance, potentially resulting in filter obstruction(13,14). A study by Tonnelier et al. demonstrated that electrostatic, HME, and mechanical filters exhibit obstruction after 24 hours of exposure to humidification and nebulization(14). However, the present study reveals no statistically significant pressure across filters among the different filter types. This observation can be explained by considering several possibilities. Primarily, it is plausible that the accumulation of aerosol and humidity within the filter was minimal owing to the brief nebulization period and the small volume utilized in the investigation. Furthermore, the ventilator configuration implemented in the present study engendered a flow rate of 30 LPM, potentially resulting in a minimal pressure gradient across the filter. This disparity contrasts with a previous inquiry in which a flow rate of 40 to 60 LPM was employed to assess the pressure gradient across the filters(12,13). Lastly, the pressure proximal and distal to the filter was measured by a pressure transducer, which showed only whole numbers without decimals. This number was continuously displayed on a monitor screen, and the maximum number was manually recorded by an investigator, not automatically recorded by the machine. Therefore, no significant difference in pressure across filters between each type of filter was seen in the present study.

The limitation of the present study is that it measures the particles of NSS aerosols in the environment rather than quantifying the amount of coronavirus contamination. Moreover, the results may not be applicable in scenarios where multiple doses of nebulization are required.

Conclusion

Nebulization is an aerosol-generating procedure that could lead to the spread of diseases, including COVID-19. The present study was designed to address this issue by using a filter attached to a nebulization kit to reduce aerosol particles passing through. The results reveal that if 5 mL of NSS was nebulized within five minutes, mechanical, electrostatic, and electrostatic filters with HME effectively decrease the number of dispersed particles in the environment. None of the filters demonstrated superiority in the filtration of NSS aerosols compared to other filters. However, filtration efficiency may vary with a more significant volume of NSS or longer durations. Further research is required to address this knowledge gap, which could help prevent the spread of aerosol-borne diseases in the future.

What is already known on this topic?

COVID-19 can spread via aerosols. Previous studies have shown that mechanical filters, electrostatic filters, and electrostatic filters with HME can significantly reduce particle dispersion into the environment.

What does this study add?

This study indicates that when nebulization is performed only once and for brief durations, mechanical, electrostatic, and electrostatic filters with HME are effective in the filtration of NSS aerosols compared to no filter.

Funding disclosure

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Conflicts of interest

The authors declare that they have no competing interests.

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