Comparison Of Different Exhalation Filters In Protection Against Fugitive Aerosol During Nebulizer Treatments: An In-vitro Study

COMPARISON OF DIFFERENT EXHALATION FILTERS IN PROTECTION AGAINST FUGITIVE AEROSOL DURING NEBULIZER TREATMENTS: AN IN-VITRO STUDY

By

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Under the supervision of Dr. Douglas S. Gardenhire

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ABSTRACT

Background: Aerosol escaping to the environment during nebulization treatments is called fugitive aerosol. Placing a filter at the exhalation outlet is one way to prevent unintended inhalation of fugitive aerosol by healthcare providers. Aim: To determine the best exhalation filter in preventing fugitive aerosol from escaping to the environment.

Methods: Three brands of exhalation filters were tested in our study, the Westmed filter, Airlife filter, and Microgard filter. They were attached at the exhalation outlet of the Circulaire II nebulizer with a collection filter sitting right after. Each filter was nebulized for three consecutive tests before being discarded. For each test, albuterol (2.5 mg/0.5 ml equivalent to 3 mg of albuterol sulfate) was nebulized to a simulated breathing adult patient (VT 500 ml, RR 15 BPM) by a flowmeter powered with 8 LPM for five minutes. After completion of each test, the collection filter was rinsed and gently stirred with 0.1N of HCl before being analyzed by a spectrophotometry device for the determination of fugitive dose.

Results: All types of exhalation filters allowed less than 0.4% of the nominal dose to escaped for each nebulization test. There were no differences in fugitive dose between each exhalation filter within the three nebulization tests (p >0.05), and the average of the three tests (p >0.05). There was also no difference in fugitive dose between each test for the same type of exhalation filter (p >0.05).

Conclusion: Regardless of the exhalation filter tested, all offer similar protection against fugitive aerosol for the first three nebulization treatments.

DEDICATION

I'm grateful for everything happening in my life. After the intense 2 years of the Integrated Master program for Respiratory Therapy, I'm finally graduating. I want to thank my family members for supporting me fully day and night. I also want to thank Ting-Hui Lin for being there whenever I'm stressed or burned out. Finally, I want to thank all my friends who have helped me and lend me hands throughout the program. We may not forever be together, but our memories will.

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CHAPTER I

INTRODUCTION

Respiratory therapists (RTs) are the most crucial healthcare workers for treating patients with respiratory-related diseases. They're trained to perform various therapies to aid patients in recovery, and delivering aerosolized treatments through nebulizers is the most common of all. While aerosolizing medications alleviate the burden of diseases for patients, healthcare workers like RTs on the other hand might potentially be harmed by unexpected exposure to them. This has always been a concern in nebulizer treatments, and methods to reduce the exposure to healthcare workers are always of interest.

THE STATEMENT OF THE QUESTION

There have been several proposed routes to reduce accidental inhalation of aerosolized drugs in different scenarios(Ari et al., 2016; James A. McGrath, O'Sullivan, et al., 2019; Tsai et al., 2015; Bart P.H. Wittgen et al., 2006), one of which is to insert a filter at the expiration port connected to a nebulizer and patient interface in simulated spontaneously breathing patients(James A. McGrath, O'Sullivan, et al., 2019). While this method looks promising, our next question is, what kind of exhalation filter protects healthcare workers best? Thus, the purpose of this study is to compare different brands of exhalation filters in preventing aerosolized drugs from contaminating the environment.

THE RATIONALE

The discussion on the occupational hazard of providing aerosol treatments has been extensively studied(Ari et al., 2016; Croteau et al., 2004; Elmashae et al., 2019; Ishau et al., 2020; James A. McGrath, O'Sullivan, et al., 2019; James A. McGrath, O'Toole, et al., 2019; O'Riordan & Smaldone, 1992; Saeed et al., 2017; Tsai et al., 2015; Bart P.H. Wittgen et al., 2006). Aerosol escaping to the environment either from the nebulizer or the patient is called fugitive aerosol. It is imperative to protect healthcare workers from inhaling fugitive aerosol containing drugs that could cause undesired side effects and the risk of developing asthma(Christiani & Kern, 1993). Especially in times like this with the pandemic of coronavirus disease 2019 (COVID19), people now seek maximum protection from hazardous aerosol more than ever. Healthcare workers not only have to worry about being exposed to aerosolized drugs, but they also have to worry about fugitive aerosol contaminated with COVID19 from the patient. There are proposed guidelines on how to safely deliver aerosol treatments to COVID19 patients, and they recommended attaching the exhalation filter to prevent contamination of the environment(Ari, 2020; Benge & Barwise, 2020). The effort of those guidelines along with previous studies is to provide healthcare workers more information about the risk of fugitive aerosol and how to prevent them, hence, knowing which type of exhalation filter that provides the most protection will prove beneficial.

THE HYPOTHESIS

We hypothesize that different brands of exhalation filters will have varying protection against fugitive aerosol during nebulizer treatments in spontaneously breathing patients. The purpose of this in-vitro study is to compare different brands of exhalation filters in protecting against fugitive dose generated by nebulizers in a simulated spontaneously breathing adult lung model.

CHAPTER II

BACKGROUND

Aerosol treatments have been used to deliver extensive varieties of drugs to patients with pulmonary conditions. From simple bland aerosol treatment to aerosolized bronchodilators and antibiotics, they are all meant to alleviate burdens of pulmonary diseases from the patient. The benefits of delivering aerosolized drugs to patients are faster onset on targeted organs and lower systemic effects. Respiratory therapists (RTs) are experts in utilizing different kinds of nebulizers that would deliver particle size mainly between 1 to 8 μm and resolve a variety of respiratory-related issues(Wang et al., 2017).

While most studies are interested in drug deposition to the patient during aerosol treatments, few have examined that did not. Aerosol generated by a nebulizer that escaped from the nebulizing system or failed to deposit in the respiratory tract and exhaled to the environment is called the fugitive aerosol. When unintentionally inhaled by bystanders such as RTs, it might cause deleterious side effects and increase the risk of developing occupational asthma accompany by familial economic crisis(Barnes et al., 1996; Blanc et al., 1999, 2003; Weiss et al., 1992). Many factors dictate the amount of fugitive aerosol contaminating the environment and threatening the health of bystanders during nebulizer treatments. Context-related key factors include interzonal airflow rate, external airflow rate, air-exchange rate, deposition rate, particle resuspension, and particle coagulation(He et al., 2005; J.A. McGrath et al., 2014a, 2014b; W. W. Nazaroff, 2004; William W Nazaroff, 2016). Nebulizer and patient-related key factors include nebulizer types, nebulizing durations, supplemental gas flow rate, patient interface, distance from the nebulizing source, and fill volume inside nebulizer(Elmashae et al., 2019; James A. McGrath, O'Sullivan, et al., 2019; James A. McGrath, O'Toole, et al., 2019; Rau et al., 2004; Saeed et al., 2017).

The topic of fugitive aerosol harming healthcare workers has always been concerning either in hospital or home care settings. Aerosolized drugs such as Pentamidine, ribavirin, Adeno-associated virus serotype 2 vector containing cystic fibrosis transmembrane conductance regulator complementary DNA, sustained-release lipid inhalation targeting cisplatin, and glutaraldehyde have all been highlighted as they are associated with occupational hazards when healthcare workers are exposed to their fugitive aerosol(Croteau et al., 2004; Dimich-Ward et al., 2004; McDiarmid et al., 1992, 1993; O'Riordan & Smaldone, 1992; Tsai et al., 2015; B. P.H. Wittgen et al., 2007). In addition to harmful drugs escaping to the environment with fugitive aerosol, infectious pathogens like influenza, mycobacterium tuberculosis, and severe acute respiratory syndrome coronavirus could also be transmitted through escaping aerosol during common oxygen therapies(Simonds et al., 2010; Tran et al., 2012). Patients in severe respiratory failure requiring invasive mechanical ventilation have compromised upper airway due to the insertion of an endotracheal tube. They are more susceptible to lower respiratory tract infection and have the potential to spread pathogens like gram-positive bacterias, gram-negative bacterias, viruses or fungi from their lungs to the ventilator circuit, then to the environment (da Silveira et al., 2019; Jaiswal et al., 2018; Kelly et al., 2016; Mitchell et al., 2018; Nazareth et al., 2020; Picazo et al., 2020; Sommerstein et al., 2019; Tsakiridou et al., 2018, p.; Zakharkina et al., 2017).

Recently, a global outbreak of coronavirus disease 2019 (COVID19) has struck the world off guard. The pathogen is transmitted through droplet and airborne(Y. Liu et al., 2020), which means patients with COVID19 needing aerosol treatments could contaminate the environment with COVID19 pathogen, carried by fugitive aerosol increasing the risk of healthcare workers being infected when rendering care. To make matter worse, shortage of N95 masks has taken a toll on healthcare providers worldwide, thus, some have proposed attaching filters onto commercially available elastomeric respirators to substitute N95 masks(D. C. Y. Liu et al., 2020). There are also guidelines proposed on how to safely deliver nebulizer treatments to COVID19 patients, and putting an exhalation filter at the expiratory port is one of the options(Ari, 2020; Benge & Barwise, 2020; Fink et al., 2020; Respiratory Care Committee of Chinese Thoracic Society, 2020). All the efforts mentioned above are to protect healthcare workers from inhaling fugitive aerosols containing COVID19 when providing therapies like aerosol treatment. This concept is similar to other studies showing less fugitive aerosol spreading to the environment when a filter is placed at the exhalation limb of a ventilator circuit

(Ari et al., 2016; O'Toole et al., 2020) or the exhalation port of a breathing system intended for nebulizer treatments (Mac Giolla Eain et al., 2021; James A. McGrath, O'Sullivan, et al., 2019), it minimizes secondary exposure to unintended personnel.

The idea of having an exhalation filter sit at the expiratory port to prevent fugitive aerosol sounds promising. To the best of our knowledge, limited data have compared different kinds of exhalation filter in their ability to minimize secondary exposure during nebulizer treatments, thus, the purpose of this article is to compare different exhalation filters in their efficiency to stop fugitive aerosol from contaminating the environment with commonly seen nebulizers in simulated spontaneously breathing patients.

CHAPTER III

RESEARCH DESIGN

This is an original article conducted in the form of a bench study. The main objective was to describe different brands of exhalation filters in their efficiency to prevent fugitive aerosol from escaping to the environment during aerosol treatments. No human subject was involved in the study, thus, no institutional review board approval was needed prior.

NEBULIZERS AND DRUG

Circulaire II available on the market of the United States (Westmed, Tucson, AZ, USA) was utilized in the study (Figure 1). Albuterol (2.5mg/3 ml, equivalent to 3mg of albuterol sulfate) (Nephron Pharmaceuticals Corporation, West Columbia, SC, USA), a common bronchodilator in clinical was the drug of choice to be nebulized.

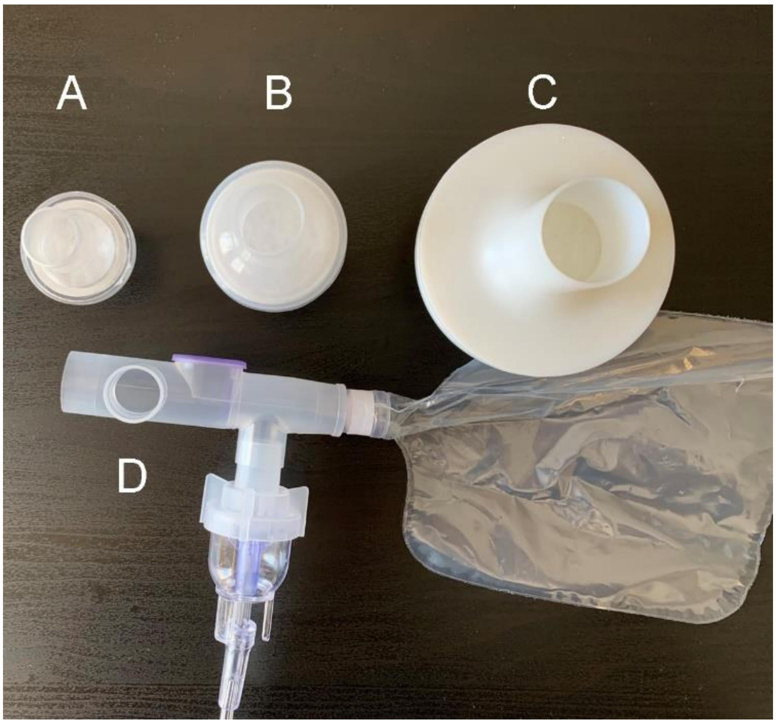
EXHALATION FILTERS

We tested 3 different exhalation filters in this study (Figure 1). The Westmed filter (Westmed, Tucson, AZ, USA) that comes with the Circulaire II package, the AirLife filter (CareFusion, Yorba Linda, CA, USA), and the MicroGard filter (CareFusion Germany, Hoechberg, Bavaria, Germany). Exhalation filters from different brands were attached appropriately to the exhalation outlet of Circulaire II, followed by a collecting filter (CareFusion, Yorba Linda, CA, USA) placed directly after the tested exhalation filter.

Aerosolized albuterol caught in the collecting filter represented fugitive aerosol that bypassed the exhalation filter and into the environment. The peep valve of Circulaire II was not used in our study.

Figure 1

Exhalation filters and nebulizer tested



The three exhalation filters and nebulizer tested are shown above. A: Westmed filter; B: Airlife filter; C: Microgard filter; D: Circulaire II

SIMULATED PATIENT MODEL

This study utilized an ASL5000 breathing simulator (IngMar Medical, Pittsburgh, PA, USA) to mimic healthy spontaneously breathing adult patients. The Circulaire II/exhalation filter complex was connected to the ASL5000 with two protection filters (CareFusion, Yorba Linda, CA, USA) in between. The settings for the ASL5000 breathing simulator were respiratory rate 15 breaths per minute, tidal volume 500 ml, lung compliance 0.05 L/cmH20, and airway resistance 6 cmH20/L/sec.

VARIABLES

There was one independent variable in this study, the different brands of exhalation filter. There was one dependent variable, the fugitive dose, expressed as the percentage of the nominal dose administered to the nebulizer.

SETTINGS

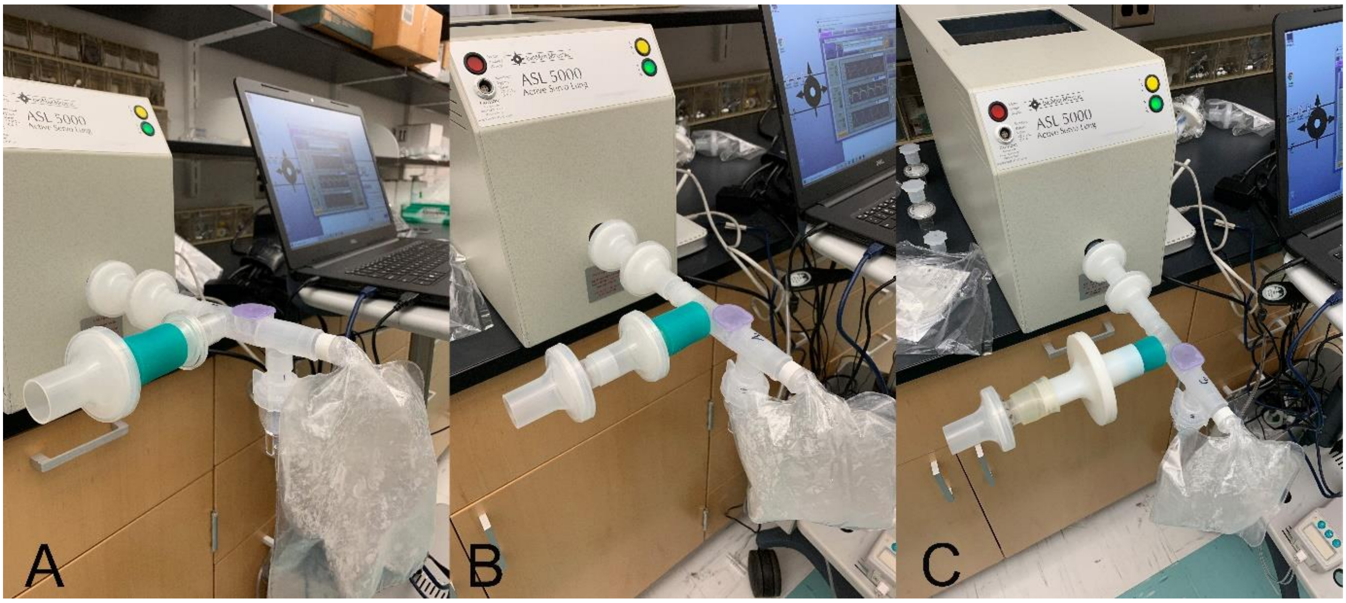
The study was carried out in the Aerosol Research Laboratory located in the Department of Respiratory Therapy at Georgia State University, United States of America.

EXPERIMENT PROTOCOL

We utilized 3 identical but separate Circulaire II and exhalation filters of each type. Each exhalation filter was tested 3 times repeatability on each Circulaire II before being discarded, which resulted in 27 nebulization trials overall. For each trial, after proper Circulaire II/exhalation filter complex setup (Figure 2), albuterol sulfate solution was administered into the jet nebulizer of Circulaire II. The jet nebulizer was powered with 8 L/min of 100% oxygen flow from a flowmeter while simultaneously activating ASL5000 for 5 minutes. After 5 minutes, the collecting filter with albuterol sulfate deposited was rinsed with 10 ml of 0.1 N hydrochloric acid (JT Baker Company, Phillipsburg, NJ, USA). To ensure proper and balanced mixing, the solution was gently stirred for 3 minutes, then collected into a cuvette. A calibrated spectrophotometry device (Beckman Instruments, Fullerton, CA, USA) ultimately measured albuterol sulfate concentration in the cuvette using the wavelength of 273 nm. By utilizing the equation 0.173*absorbance*10/3, it will give us the amount of albuterol sulfate captured (in mg). Since each Circulaire II/exhalation filter experiment was repeated 3 times, and conducted on 3 separate Circulaire, it gave us 3 independent experiments (n=3).

Figure 2

Illustration of Circulaire II/exhalation filter setup

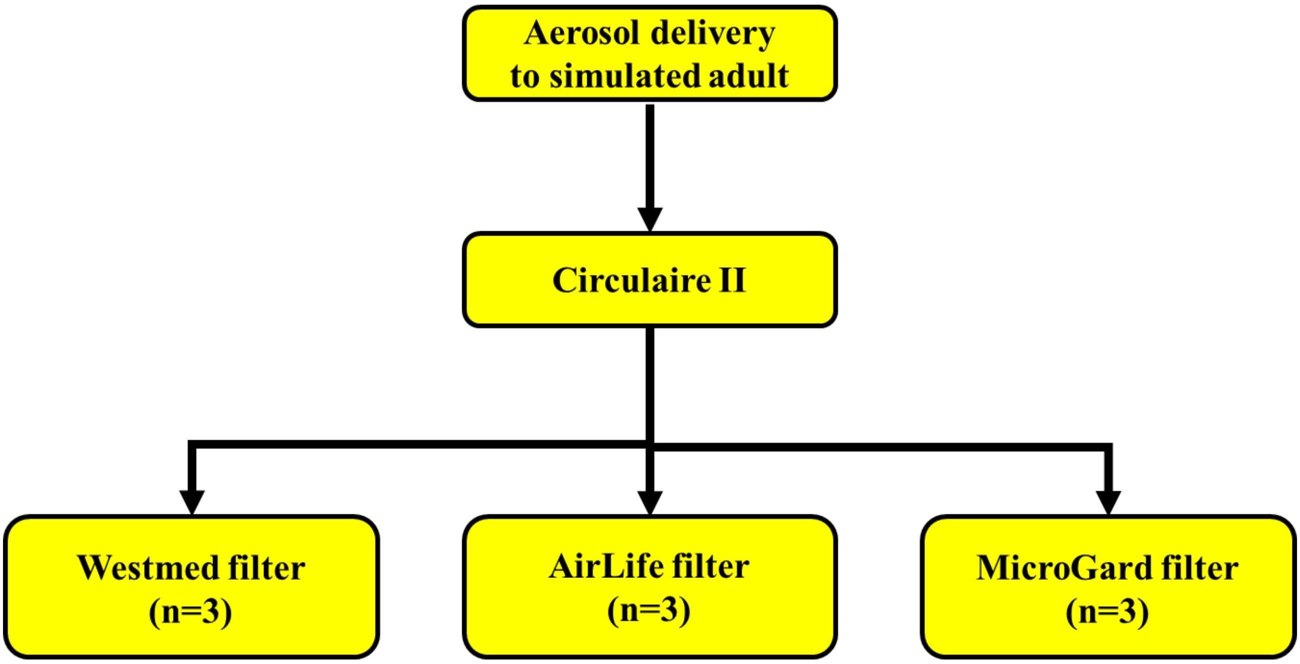


The experimental setup for A) Westmed filter, B) Airlife filter, and C) Microgard filter are shown above.

DATA COLLECTION

Figure 3

Experimental outline for this study



A diagram showing the outline of experiments in the study

STATISTICAL ANALYSIS

The Statistical Package For The Social Sciences (SPSS) 27th version (IBM Corp., Armonk, NY, USA, 2020) was used for the analysis of the study. Utilizing descriptive analysis, the fugitive dose was expressed as the percentage ± SE of the nominal dose administered to the nebulizer. One-way analysis of variance (ANOVA) was used to compare differences in fugitive dose among different brands of exhalation filter, while repeated-measures ANOVA was used for the comparison of the same exhalation filter. The Bonferroni correction was used for the post-hoc test. A *p*-value of less than 0.05 was considered to be statistically significant.

DATA MANAGEMENT AND STORAGE

Study data collected were all stored in a computer database (SPSS). A codebook was created before data entry to ensure accurate and reliable study results. The computer used for data storage had restricted access strictly to researchers related to the study by passwords. The Data Management Advisory Team (DMAT) of Georgia State University was available during the time of study to assist in the protection and management of the data.

CHAPTER IV

RESULTS

Table 1 shows the fugitive dose (mean±SE in percent of nominal dose**)** for each exhalation filter in each test and the average of 3 tests. Raw data for our study could be found in Supplemental Table 1 in appendices.

COMPARISON OF FUGITIVE DOSE IN EACH TEST BETWEEN EXHALATION FILTERS

To determine if there's a difference in filter protection efficiency after exposure to multiple nebulization tests (3 for this study), one-way ANOVA was utilized to compare the fugitive dose of each test between different brands of exhalation filter. The findings of this study showed no difference in the protection efficiency between exhalation filters during each nebulization test [F(2, 6) = 0.362, *p*=0.710, for 1st test] [F(2, 6) = 1.041, *p*=0.409, for 2nd test] [F(2, 6) = 4.436, *p*=0.066, for 3rd test].

COMPARISON OF MEAN FUGITIVE DOSE BETWEEN EXHALATION FILTERS

To contrast the overall protection efficiency of each exhalation filter, we calculated the mean fugitive dose for the 3 tests of each exhalation filter and utilized one-way ANOVA for comparison. Our results showed no difference in the overall protection efficiency between exhalation filters [F(2, 6) = 1.717, *p*=0.257].

COMPARISON OF FUGITIVE DOSE BETWEEN EACH TEST FOR THE SAME FILTER TYPE

Clinically, the same nebulizer/exhalation filter complex would be used several times before being discarded. To determine if the filter protection efficiency would differ after each nebulization test (up to 3 in this study), we utilized repeated-measure ANOVA. Our findings showed no difference in filter protection efficiency between each test for the same filter type [$F(1, 2) = 3.441$, $p = 0.205$, for Westmed filter] [$F(2, 4) = 1.998$, $p = 0.250$, for Airlife filter] [$F(2, 4) = 1.176$, $p = 0.397$, for Microgard filter].

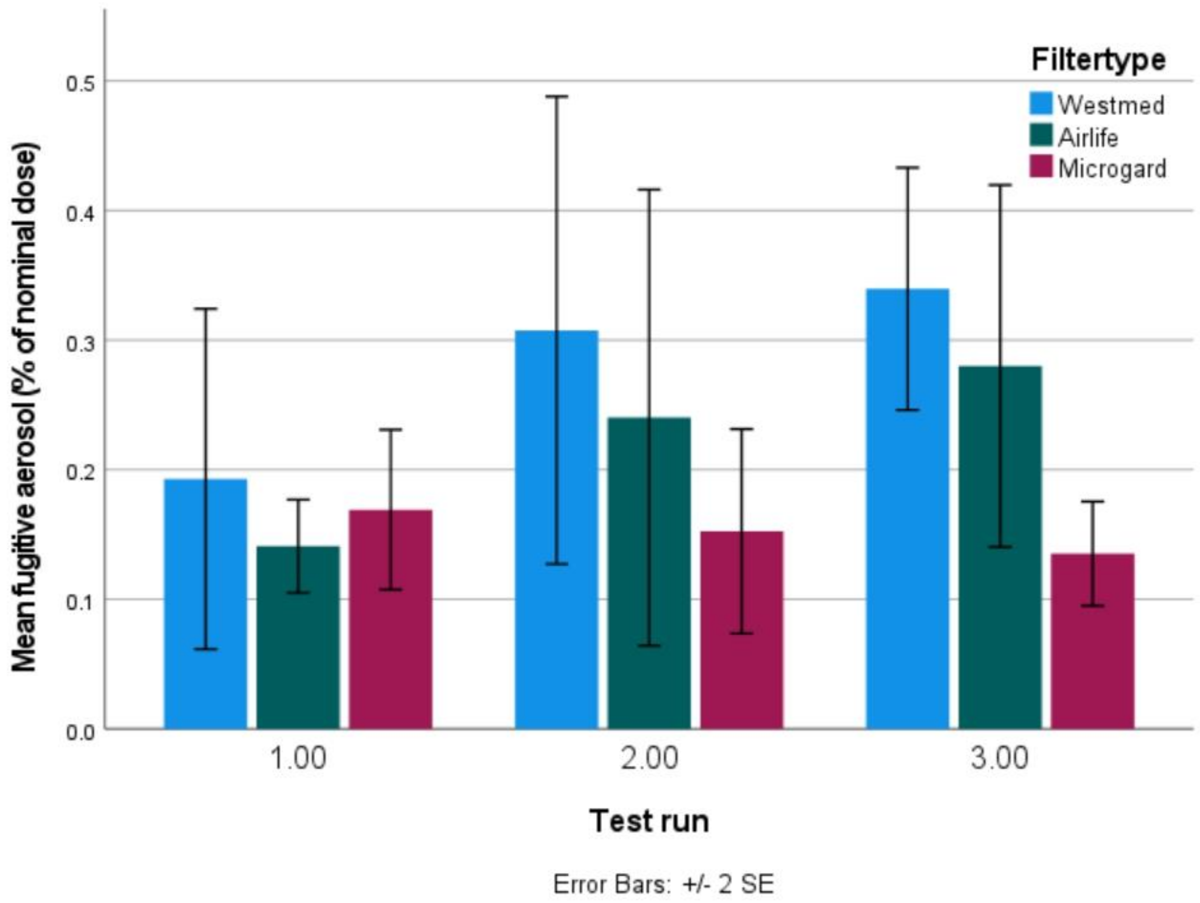
Table 1

Fugitive dose expressed in percent of nominal dose (mean±SE) for each type of exhalation filter. The mean fugitive dose for 3 repeated tests of each filter is also calculated.

Circulaire II				
Measurement / Filter type	Fugitive dose on 1st test	Fugitive dose on 2nd test	Fugitive dose on 3rd test	Mean fugitive dose
Westmed filter	0.19±0.1%	0.31±0.1%	0.34±0.1%	0.28±0.1%
Airlife filter	0.14±0.0%	0.24±0.1%	0.28±0.1%	0.22±0.1%
Microgard filter	0.17±0.0%	0.15±0.0%	0.14±0.0%	0.15±0.0%

Figure 4

Fugitive aerosol among three exhalation filters during each test run



Fugitive aerosol escaping to the environment among the three exhalation filters for each test run are shown above (error bars show ±2 standard errors).

CHAPTER V

DISCUSSION

Patients have the right to receive proper treatments to ease the burden of diseases, while healthcare providers have the right to be free of harm during the process of delivering care, and that includes aerosol treatments. The idea of providing therapeutic aerosol to patients in need is justifiable, but how we protect bystanders such as RTs from fugitive aerosol remains a true question. We know placing an exhalation filter during nebulizer treatment would protect the surrounding environment from fugitive aerosol (Ari et al., 2016; Mac Giolla Eain et al., 2021; O'Toole et al., 2020), but different brands of exhalation filters would have varying protection efficiency, thus, this study intends to find the best exhalation filter regarding protection efficiency. According to our results, an average of less than 0.4% of albuterol nominal dose escaped to the environment for all types of tested exhalation filters during the first three nebulization trials. We demonstrated trends of increasing fugitive dose after each nebulization test for Westmed and Airlife filter, while Microgard presented the opposite, though all were not statistically significant (Table 1). After averaging the fugitive dose from three nebulization tests, the Westmed filter allowed almost twice the amount of fugitive aerosol to escaped comparing to the Microgard filter, again, it wasn't statistically significant (Table 1). To the best of our knowledge, no study that investigates the protection efficiency from aerosolized drugs between different exhalation filters has been published so far, thus, we can not compare our results with other similar studies.

While most studies focus on the amount of aerosolized drug delivered to the patient, few have looked into the fugitive aerosol hazard. Interestingly, one study found around 30% of albuterol nominal doses escaped to the environment during jet nebulization therapy for spontaneously breathing patients without an exhalation filter in place (James A. McGrath, O'Sullivan, et al., 2019). Another study that utilized Circulaire II to nebulized albuterol also found around 12% of the nominal dose escaping to the environment without an exhalation filter at the exhalation outlet (Rau et al., 2004). Their results underline the importance of exhalation filters, which in our study, only less than 0.4% of nominal dose were allowed to escape with exhalation filter inserted, regardless of the type of exhalation filter.

According to different sources, the occupational exposure limit for albuterol stands between 2 mcg/day (Frank et al., 2019) to 10 mcg/8 hr (Nephron Pharmaceuticals, 2021). The observed fugitive aerosol for our study stands between 2.48 mcg to 14.5 mcg for each nebulization test, with an average of 4.6 mcg to 8.4 mcg overall throughout the 3 tested exhalation filters (Supplemental Table 1). These fugitive dosages are obtained right at the exhalation outlet of the Circulaire II, and there is a list of factors that would dictate the amount of accidental inhalation by healthcare workers nearby, such as context-related, nebulizer-related, and patient-related key factors, as stated earlier (Elmashae et al., 2019; He et al., 2005; J.A. McGrath et al., 2014a; James A. McGrath, O'Toole, et al., 2019; W. W. Nazaroff, 2004; William W Nazaroff, 2016; Rau et al., 2004; Saeed et al., 2017). Since there were no differences in protection efficiency of the three tested exhalation filters for the first 3 nebulization run, the safest method to minimize occupational exposure to aerosolized drugs is simply ensuring the placement of an exhalation filter for every patient, regardless of type, and changing them every day for optimal protection efficiency as most patients would only need an average of 3 to 4 nebulization treatments per day.

CLINICAL IMPLICATIONS

It is crucial to protect healthcare workers from inhaling excessive fugitive aerosol generated by nebulizer treatments, which is why it is vital to find the best exhalation filter that provides the most protection. This study demonstrated similar protection efficiency among the three tested exhalation filters during the first three nebulizer treatments for spontaneously breathing patients. Therefore, with the evidence provided by our study, it is safe to utilize any of the three tested exhalation filters without having to worry about inferior protection ability, given the filter is changed every day.

SUGGESTIONS FOR FUTURE RESEARCH

Future studies should incorporate more brands of exhalation filters to compare, as our study only utilized three commonly seen ones in the USA market. More nebulization tests for each exhalation filter should be conducted to simulate the clinical scenarios of more severe patients, who would need more frequent aerosol treatments per day (i.e. more than three).

LIMITATION

Our study has several limitations. Since it is an in-vitro study, the data gathered can not fully represent the ever-changing clinical context. For instance, the simulated lung model can not represent a real patient with different breathing patterns, tidal volume, lung characteristics, or anatomy. Nebulizers and exhalation filters used in our study can not represent all other varieties in the market. Finally, results from utilizing albuterol sulfate in our study can not represent all other drug formulations, as different drugs have distinct aerosol dynamics.

CONCLUSION

The topic of occupational exposure to fugitive aerosol in healthcare environments has always been a concern. There are various methods to minimize fugitive aerosol, and placing a filter at the exhalation outlet of a nebulizer is one of them. According to our study results, there were no differences in the protection ability between the three tested filters within the first three nebulization tests and the average of them. Our findings also showed similar protection efficiency between each test run for the same type of exhalation filter. In conclusion, it is safe to utilize any of the three tested exhalation filters during aerosol treatments as they provide comparable protection against fugitive aerosol.

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APPENDICES

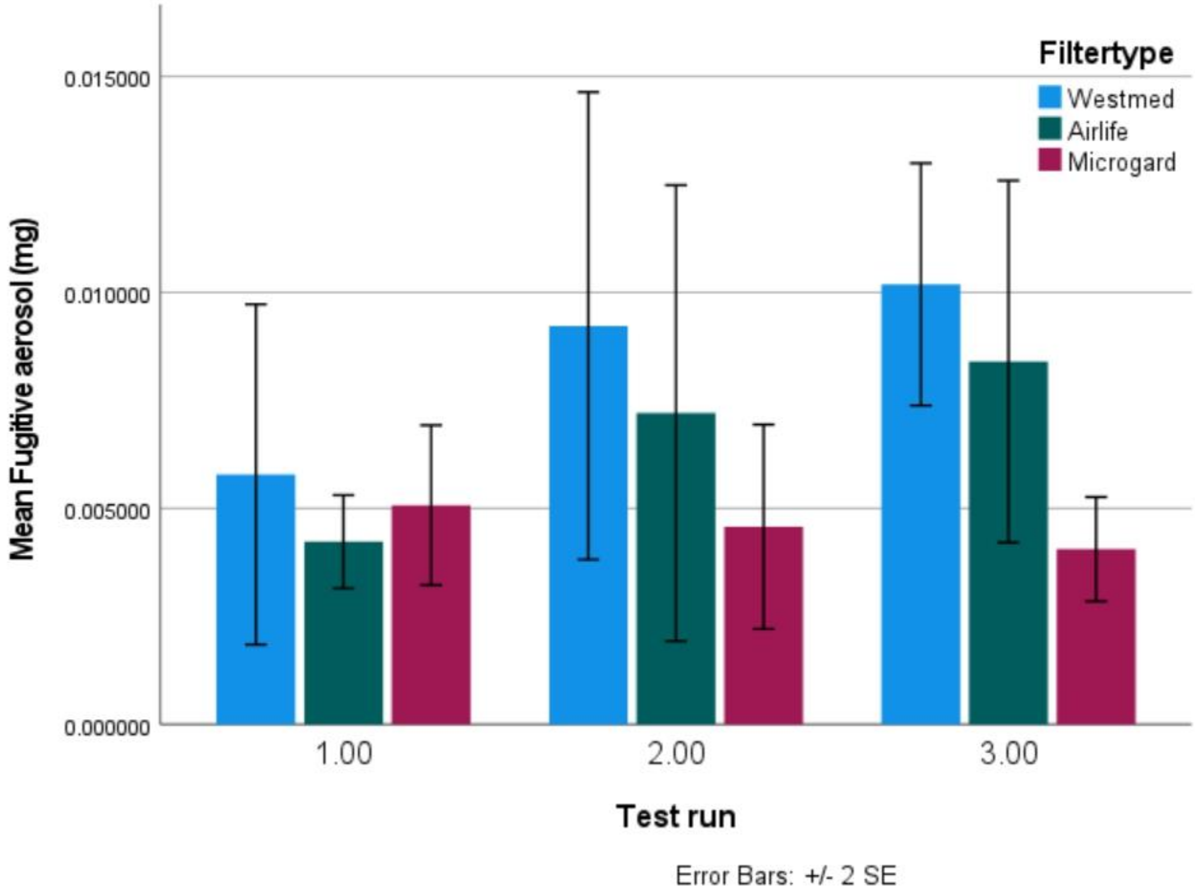
Supplemental Table 1

Raw data for our study. Fugitive doses in mg are shown for each exhalation filter in the respective nebulization test and the average of 3 tests.

Filter type	Nebulizer number	Fugitive dose on 1st test (mg)	Fugitive dose on 2nd test (mg)	Fugitive dose on 3rd test (mg)	Mean fugitive dose (mg)	
Westmed	1	.00548	.00750	.01223	.00840	0.008400111
	2	.00934	.01453	.01084	.01157	
	3	.00254	.00565	.00750	.00523	
Airlife	1	.00363	.00409	.00565	.00446	0.006612444
	2	.00375	.01246	.01251	.00957	
	3	.00531	.00508	.00704	.00581	
Microgard	1	.00611	.00657	.00421	.00563	0.004568481
	2	.00323	.00248	.00294	.00288	
	3	.00588	.00467	.00502	.00519	

Supplemental Figure 1

Fugitive aerosol among three exhalation filters during each test run



Fugitive aerosol escaping to the environment among the three exhalation filters for each test run are shown above (error bars show ±2 standard errors).