The impact of aerosolized mucolytic agents on the airflow resistance of bacterial filters used in mechanical ventilation

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Background/Purpose: In order to reduce the contamination in the ventilator, bacterial filters were placed on the expiratory limb of a ventilator circuit. Aerosolized mucolytic agents may increase the resistance of the ventilator. The goal of this study is to determine the impact of aerosolized mucolytic agents on the pressure change during mechanical ventilation.

Methods: A lung model was investigated with mucolytic inhaled agents of 10% acetylcysteine and 2% hypertonic saline. The agents were administered using a jet nebulizer every 45 minutes for 15 minutes. The pressure drop was measured after nebulization. The end point was referred to the 45th dose or obstruction of the filter. Furthermore, the pressure drop after steam autoclaving was also measured.

Results: The maximum pressure was significantly higher with 10% acetylcysteine than with 2% sodium chloride (39.32 ± 7.22 cmH2O vs. 3.53 ± 0.90 cmH2O, p < 0.001). With acetylcysteine filters, the pressure drop over 4 cmH2O occurred earlier and had a good relationship between the degree of pressure drop and doses. The acetylcysteine group yielded a significant difference in the pressure drop compared to the newly autoclaved and the end point of inhalation (p = 0.043).
Conclusion: This study demonstrated the aerosolized mucolytic agents could increase the pressure drop of the bacterial filters during mechanical ventilation. The pressure drop of the bacterial filters was higher with 10% acetylcysteine. It is critical to continuously monitor the expiration resistance, auto-positive end-expiratory pressure, and ventilator output waveform when aerosolized 10% acetylcysteine was used in mechanical ventilation patients.

Introduction

Breathing system filters are expected to prevent the transmission of microbes and other particulate substance in breathing systems when the patient’s upper airway has been bypassed during anesthesia and intensive care. In order to reduce the risk of contaminating the ventilator when mechanically ventilating a patient with suspected or confirmed infectious disease, a bacterial filter was placed on the expiratory limb of the breathing circuit of a ventilator.

Aerosolization of medications is the optimal route of administration for some pulmonary diseases. Many aerosolized medications could be administered after nebulization, such as bronchodilators, steroid, antibiotics, hypertonic saline, and mucolytic agents. Jet nebulizer can be used during mechanical ventilation. The jet nebulizer functions by passing compressed gas through a narrow orifice and creating an area of low pressure at the outlet of the adjacent liquid feed tube. This results in the drug solution being drawn up from the fluid reservoir, which then shatters into droplets in the gas stream.

There is a potential adverse effect that aerosolized particles can accumulate on the bacterial filter, increasing the resistance to restrict the patient’s normal breathing pattern. Some adverse reports indicated that the nebulization treatment caused the malfunction of the exhalation valve or bacterial filter and patients could not exhale properly. A previous study had reported that the bacterial filter in a nebulizing system with bronchodilator treatment such as salbutamol and ipratropium could be safely employed. However, to the best of our knowledge, there is very little research on nebulized mucolytic agents. The goal of this study is to determine the impact of aerosolized mucolytic agents on the bacterial filter during mechanical ventilation.

Materials and methods

Lung model and ventilator settings

To simulate the adult mechanical ventilation, the ventilator (Galileo, Hamilton Medical, Switzerland) settings were adjusted as follows: a tidal volume of 0.6 L, a respiratory rate of 12 b/min, an inspiratory time of 1 second, positive end-expiratory pressure (PEEP) of 5 cmH₂O, and an inspiratory flow rate of 54 L/min in a descending ramp flow pattern. The ventilator alarm was set at a pressure of more than 45 cmH₂O, which implied that the filter would be obstructed. This model included a ventilator circuit, a combined heat and moisture exchanger filter (Fig. 1, collection filter) (Hygrobac S, Tyco Healthcare, Italy), and a test lung (Training/Test Lung (TTL) Michigan Instruments, Grand Rapids, Michigan) with lung mechanics of 0.05 L/cmH₂O compliance and 20 cmH₂O/L/s resistance (Rp20 resistor; Fig. 1).

Filter and nebulizer

The brand new pleated hydrophobic filters (OmniFilter Tyco Healthcare Eastern and Central Europe, Puritan-Bennett Corporation, Pleasanton, CA, USA, diameter of 3.5 in., surface area of around 62.2 cm²) were located in the exhalation limb closed to the ventilator (Fig. 1, exhalation bacterial filter). The nebulizer was placed 6 in. from the Y-piece adapter, using standard attachment corrugated tubing (Fig. 1, aerosol generator). The aerosol generator used here was a jet nebulizer (Neb-Easy Nebulizer Kit, GaleMed, Wu-Jia, I-Lan, Taiwan). This device was fabricated from acrylic and polypropylene plastics; it was operated under the Venturi principle and was refillable. The nebulizer had several attachments that came with it during the nebulization process. These included a Tee connector, which connected to the top of the nebulizer; and a 6-inch corrugated tube, which connected to the side of the Tee connector. A standard oxygen tube is connected to the bottom of the nebulizer, which connected the nebulizer to a pressurized gas source.
Mucolytic agents, doses, and generator operation

Two types of mucolytic agents, 10% acetylcysteine and 2% sodium chloride (hypertonic saline), were examined. The inhaled agents were administered using a constant output jet nebulizer every 45 minutes for 15 minutes. The aerosols were administered sequentially without interruption. The nebulizer was driven by oxygen at a flow of 6 L/min. The administered agents in the two experimental groups were 10% acetylcysteine 3 mL/amp diluted with 1 mL of 0.45% sodium chloride, and 4 mL of 2% sodium chloride. The aerosol flow to the filters was kept constant by adjusting the dosage.

In vitro measurements

Pressure drop is defined as the difference of the pressures between filter inlet and outlet. The pressure drop was measured against an air flow at 100 L/min by a flow analyzer (PF 300, imtmedical, Buchs, Switzerland) prior to and after each test. Furthermore, the pressure drop was measured at 5 minute, 15 minute, and 30 minute points after 15 minutes of nebulization. The end point was referred to the 45th dose through the nebulizer or when the filter was obstructed as indicated by the ventilator alarm. Furthermore, the pressure drop after steam autoclaving was also measured.

Data analysis

Student t test or Mann-Whitney U test (Wilcoxon rank-sum test) were used to analyze the variance of pressure drop for filters. The differences in pressure drop between the baseline, the end point, and after steam autoclaving were tested with Wilcoxon signed-rank test. Pearson correlation test was used to determine if there was a correlation between the increases in pressure drop and dosage. Linear regression was used to predict the pressure drop for one dosage as a function of pressure drop. The statistic software package SPSS version 17 (SPSS Inc., Chicago, IL, USA) was used for all analysis, and p < 0.05 was considered significant.

Results

Table 1 shows the pressure change through the filters with two types of aerosolized agents, 10% acetylcysteine and 2% sodium chloride. Five filters with nebulized 10% acetylcysteine and two filters with nebulized 2% sodium chloride were examined. Prior to nebulization, the baseline pressure was recorded for each filter. After starting nebulization, pressure was recorded after each dose till the end point in each filter. The baseline and maximum pressure with these two types of aerosolized agents are summarized in Table 1. With both aerosolized agents, the pressure change was found to increase significantly after nebulization [interquartile range (IQR): 2.46–9.00 cmH2O, p = 0.013 in 10% acetylcysteine and 2.29–3.03 cmH2O, p < 0.001 in 2% sodium chloride]. In addition, the maximum pressure was significantly higher with 10% acetylcysteine than that with 2% sodium chloride (39.32 ± 7.22 cmH2O vs. 3.53 ± 0.90 cmH2O, p < 0.001).

Fig. 2 reveals the degree of pressure drop in each filter under different dosages. For the 2% sodium chloride filters (S1 and S2), the degree of pressure drop was less than 4 cmH2O even with the 45th dose. However, for the 10% acetylcysteine filters (A1–A5), the degree of pressure drop over 4 cmH2O was reached between the 10th and 17th doses. Furthermore, Fig. 3 shows a good relationship between the degree of pressure drop below 4 cmH2O and the dosage (r = 0.897–0.985, r2 = 0.805–0.97, p < 0.001) in 10% acetylcysteine filters.

Discussion

This study demonstrated that the aerosolized agents, 10% acetylcysteine and 2% sodium chloride, could increase the...
resistance of the filters through the circuit of mechanical ventilation. However, the pressure drop over 4 cmH2O through the filters was significant with 10% acetylcysteine but not with 2% sodium chloride. The pressure drop over 4 cmH2O with 10% acetylcysteine was between the 10th and 17th dosages. After steam autoclaving, the pressure drop of the filters was significantly restored in 10% acetylcysteine filters, but not in the 2% sodium chloride group.

Most studies in breathing system filters emphasized filtration and penetration performance and the efficiency of reducing the nosocomial infection rate. If the bacterial filters were obstructed by the aerosolized particles, the increased resistance of bacterial filters in the ventilator circuit would increase the airway resistance and work of breathing on patients with mechanical ventilation. Studies have indicated that the pleated hydrophobic filter was superior to the electrostatic filter in terms of bacterial and viral filtration performance and the prevention of liquid from passing through the filter layer. Breathing system filters are intended to reduce the transmission of microbes between the patient and the breathing system, and vice versa. The pleated hydrophobic filters can be placed in the breathing circuit in different positions. First, it can be placed at the inhaled branch to avoid infection of the patient from the contaminated gas coming from the ventilator. Second, it can be positioned at the exhaled branch to avoid the contamination of the patient by retrograde spread of microorganisms from the expiratory valve of the ventilator. Third, it can be placed in between the Y-connector and endotracheal tube to achieve the above two objectives. The reusable pleated hydrophobic filter was designed as an exhalation filter in a heated exhalation system in this study.

A previous study reported that bacterial filter in a nebulizing system could be safely used with the inhalation therapy of bronchodilators such as salbutamol and ipratropium bromide. The characters of mucolytic agents such as particle size, osmolarity, and viscosity were different to the bronchodilator. To the best of our knowledge, there is very little research on the effect of inhaled mucolytic agents, such as acetylcysteine, on the intubated patient. One case report revealed the risk of increasing filter resistance by mucolytic agents such as acetylcysteine with higher expiration resistance during mechanical ventilation. According to the manufacturer’s instructions of the bacterial filter, they recommended the periodic changing of the filter in 15 days and sterilization of the filters through steam autoclaving. If regularly and consistently administered nebulization therapy is given three times a day for 15 days, the filter will endure the maximum of 45 times of nebulization treatment. This manufacturer’s instruction also suggests that it is critical to inspect and check the pressure drop across the filter prior to every reuse and the maximum allowable pressure drop across the filter is below 4 cmH2O at 100 L/min. In our study, it has been observed that both 10% acetylcysteine and 2% hypertonic saline inhalation agents would increase the pressure drop across an exhalation filter. Throughout the entire testing process, all five of the 10% acetylcysteine filters were obstructed by the particles prior to the 45th dose but not in two of the 2% sodium chloride group.

The test mucolytic agent, 10% acetylcysteine solution, had a special odor and sticky appearance. Throughout the entire study, the filters were inspected prior to the pressure drop was checked. After multiple application, there was some sticky substance coating inside the 10% acetylcysteine filters and it appeared stickier than its original form. The group of 2% sodium chloride filters was found to be coated inside with some white powdery substance. A previous study reported that the pressure drop across the filters...
would be significantly increased if the testing dosage increased and the penetration performance decreased. The causes of the dramatically increasing pressure drop across the filter by the nebulized 10% acetylcysteine might be related to the quality and quantity of the solution.

In this study, the pressure drop of all the tested filters was decreased after steam autoclaving. However, the 10% acetylcysteine filters’ pressure drop could not return to the manufacturer’s recommended value of less than 4 cmH2O. It means that even if the pressure drop is better, the functioning of the filter gets affected. This was because those filters were already significantly obstructed by aerosol particles. The clinical implication is that it is critical to continuously monitor the patient’s expiration resistance, auto PEEP, and ventilator output waveform for early detection of any related filter plugging, and to sterilize or replace the filter accordingly.

There were some limitations in this study. First, the mechanical ventilator settings in this study were all constant with the fixed tidal volume, respiratory rate, inspiratory time, and flow rate. However, the parameters of mechanical ventilator setting are variable in clinical practice and probable to influence the performance of filters. Second, the interval between courses of nebulization therapy in this study was shorter than that in usual clinical practice. The interval between courses of inhalation therapy was 45 minutes in the present study. However, in general clinical practice, the frequency of nebulization mucolytic therapy is 2–3 times per day, and the interval is every 6–12 hours. Third, the characteristics of the nebulization agent such as osmolarity and aerosol particle size were not addressed in this in vitro study. These factors would be important to influence the filter resistance. Finally, this was a lung model study and direct application of these data to the clinical practice is limited. It is necessary to further confirm the observation in this study in clinical settings.

In conclusion, the aerosolized mucolytic agent inhalation via jet continuous output nebulizer would increase the resistance of the bacterial filters at the end of exhalation limb during mechanical ventilation. The resistance of the bacterial filters after aerosolized inhalation was significantly increased with 10% acetylcysteine agent than with 2% sodium chloride agent and the filters are still out of function even after steam autoclaving. In clinical practice, it is critical to continuously monitor the expiration resistance, auto PEEP, and ventilator output waveform when aerosolized 10% acetylcysteine was used in patients with mechanical ventilation.

References
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