Peak Expiratory Flow During Mechanical Insufflation-Exsufflation: Endotracheal Tube Versus Face Mask

Sung Eun Hyun, Sang-Min Lee, and Hyung-Ik Shin

BACKGROUND: Mechanical insufflation-exsufflation (MI-E) applied through the endotracheal tube (ETT) can effectively eliminate airway secretions in intubated patients. However, the effect of the interface (ETT vs face mask) on expiratory air flow generated by MI-E has not been investigated. This study aimed to investigate the effect of the ETT on peak expiratory flow (PEF) along with other associated factors that could influence PEF generated by MI-E. METHODS: Intubated participants received 2 sessions of MI-E via ETT therapy per d for 2 consecutive days. One MI-E session consisted of 5 sets of either constant (+40/−40 cm H_2O) or incremental (+30/−30 to +50/−50 cm H_2O) pressure applications. Following extubation, MI-E sessions were repeated using face mask. Expiratory air flow during MI-E therapy was continuously measured, and every PEF during each application was analyzed using linear mixed-effect and generalized linear mixed models. RESULTS: A total of 12 participants (9 [75.0%] men; mean [SD] age, 74.0 [10.2] y) completed all MI-E sessions with both ETT and face mask interfaces. The PEF generated during MI-E treatment was influenced by the interface (ETT vs face mask), pressure gradient, and number of session repetitions. Adjusted mean PEF values for MI-E via ETT and face mask at +40/−40 cm H_2O were −2.521 and −3.114 L/s, respectively, and −2.956 and −3.364 L/s at +50/−50 cm H_2O, respectively. At a pressure gradient of +40/−40 cm H_2O, only 172 of 528 MI-E trials via ETT (32.6%) achieved a PEF faster than −2.7 L/s, whereas 304 of 343 MI-E trials via face mask (88.6%) exceeded PEF < −2.7 L/s. CONCLUSIONS: MI-E via ETT generated slower PEF than via face mask, suggesting that a higher-pressure protocol should be prescribed for intubated patients. An insufflation-exsufflation pressure up to +50/−50 cm H_2O could be considered to produce a PEF faster than 2.7 L/s, and the applications were safe and feasible for subjects on invasive mechanical ventilation. *Key words: mechanical insufflation-exsufflation; cough assist; expiratory flow; endotracheal tube; mechanical ventilation; respiratory therapy.* [Respir Care 2021;66(12):1815–1823. © 2021 Daedalus Enterprises]

Introduction

Patients in the ICU receiving mechanical ventilation often require removal of airway secretions. Accumulated mucus, without timely removal, aggravates airway obstruction that can induce hypoxemia, hypoventilation, atelectasis, and ventilator-associated pneumonia.[1] Acute pulmonary infections and impaired mucociliary transport due to prolonged immobility, in addition to the use of sedatives, worsen the accumulation of large amounts of airway secretions in critically ill patients.[2]

Endotracheal suctioning through the endotracheal tube (ETT) has been commonly applied to maintain airway hygiene in the ICU. However, only the secretions from the larger proximal airways can be cleared using endotracheal suctioning because negative pressure can only be directly applied within a limited area of the bronchial tree.[2,3] Mechanical insufflation-exsufflation (MI-E) inflates the lungs using positive pressure and then abruptly shifts to negative pressure across all airways to simulate the physiologic cough, which facilitates the movement of secretions from the peripheral to the central airways.[4] Application of MI-E in the ICU could be another strategy to effectively remove secretions in intubated patients[5-7]; however, there is insufficient evidence regarding the efficiency of sputum removal using MI-E compared with conventional endotracheal suctioning. Previous studies have used different outcome measures and have drawn inconsistent conclusions about the effectiveness of MI-E in the ICU.[8,9] Additionally, the applied insufflation-exsufflation pressures ranged from +30/−30 cm H_2O to +50/−50 cm H_2O with no consensus regarding the optimal pressure settings.[3,10-12] These differences in protocol hinder current research on the effectiveness of MI-E during critical care.

The ETT interface can reduce the diameter of the main bronchi and increase total airway resistance, which might result in slower expiratory airway flow compared with the face mask interface.[13] However, the effect of the ETT on expiratory air flow during MI-E therapy has not yet been examined. In this study, we compared peak expiratory flow (PEF) during MI-E therapy through the ETT before extubation, and through face mask after extubation, in the same participants. Through these comparisons, we investigated the effect of the ETT on PEF along with other associated factors that could influence PEF generated by MI-E. The results of this study are expected to provide evidence upon which to base future protocols for MI-E therapy in intubated patients.

QUICK LOOK

Current knowledge

Mechanical insufflation-exsufflation (MI-E) improves secretion clearance through artificial airways as well as through face masks. However, wide variations in the settings have been prescribed for MI-E via the endotracheal tube (ETT) without suggesting which pressure is sufficient to reach PEF < -2.7 L/s, which has been regarded as an efficient cough generated by MI-E.

What this paper contributes to our knowledge

The use of MI-E via ETT was safe and feasible in invasively ventilated subjects in the ICU. Generated peak expiratory flow was significantly lower through the ETT than through a face mask, and a higher-pressure protocol should be considered for intubated patients. An insufflation-exsufflation pressure +50/−50 cm H_2O was necessary to reach PEF −2.7 L/s for efficient cough through ETT using MI-E.

Methods

Study Participants

We recruited patients receiving mechanical ventilation in the ICUs of a single tertiary center hospital who required MI-E therapy owing to large amount of secretions, that is, patients who needed endotracheal suctioning via ETT more frequently than every 6 h. Although endotracheal suctioning is necessary whenever clinically indicated to remove secretions, frequent suctioning (> 6 times per d) is known to increase the possibility of adverse events like hypoxemia, hemorrhagic secretions, and blood pressure or heart rate change.[14] When the patients lacked effective cough capacity and had abundant secretions, extubation had to be postponed due to a high risk of postextubation respiratory failure and re-intubation[1,2]; thus, MI-E was applied to remove secretions and maintain proper airway patency.

From June 2019 to July 2020, a total of 457 patients were consulted for ICU rehabilitation treatment, and only intubated patients on any mode of ventilation without planning extubation within the next 24 h were recruited for MI-E therapy through ETT ($n = 242$). Patients deemed too unstable for MI-E therapy initiation (PEEP > 8 cm H_2O, ratio of P_{aO_2} to F_{IO_2} < 150 mm Hg, breathing frequency > 35 breaths/min, heart rate (HR) > 130 beats/min, systolic blood pressure < 90 or > 160 mm Hg, and diastolic blood pressure < 50 or > 110 mm Hg) ($n = 64$); patients with contraindications to MI-E such as active communicable respiratory infections, barotrauma, or pneumothorax within 1 month ($n = 52$); and patients who declined or were unable to participate ($n = 78$) were excluded from the study (e-Figure 1 of the supplementary material, available at http://www.rcjournal.com).[10,15,16] A total of 21 subjects were enrolled as participants in the study to receive MI-E therapy through ETT and face mask. The institutional review board of the Ethical Committee of Seoul National University Hospital approved and monitored the study in accordance with the Declaration of Helsinki (IRB no. 1905–034–1034).

MI-E Protocol

After obtaining informed consents from the participants or their legal guardians who were substitute decision makers, each participant was scheduled for 2 MI-E sessions via ETT

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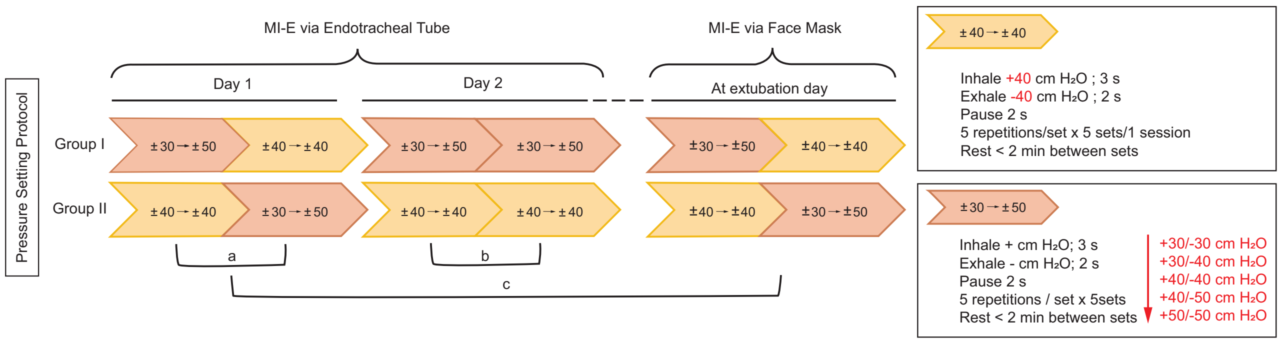

Fig. 1. Flow chart of the study to evaluate correlating factors with generated peak expiratory flow (PEF) from mechanical insufflation-exsufflation (MI-E). A: comparison of PEF based on the applied pressure, B: comparison of PEF based on the increasing number of treatment sessions, and C: comparison of PEF based on the interface (endotracheal tube vs face mask).

therapy per d for 2 consecutive days. The participants were divided into 2 groups (details are presented in Fig. 1). In group I, the pressure was increased from +30/−30 to +50/−50 cm H_2O in the first MI-E session; in group II, a constant pressure of +40/−40 cm H_2O was used for the entire first session. For the second session on day 1, the pressure settings were reversed for each group to evaluate the effect of different pressure application strategies (constant vs incremental) on air flow generated through the ETT in the same participants (Figure 1a). The same pressure settings as those used in the first session on d 1 were applied for both sessions on d 2 to evaluate the effects of the number of MI-E treatment sessions on air flow (Figure 1b). Since the timing of extubation varied according to individual medical conditions, not all participants completed 4 sessions of MI-E with flow measurements. If the extubation was successfully performed before the initial 4 successive MI-E sessions, only completed flow measurements were included in the analysis. However, participants who remained intubated after 4 sessions were continued on MI-E treatment via the ETT until extubated using incremental pressure settings. MI-E treatments after the initial 4 sessions during the intubation period were neither measured nor included in the analysis.

After extubation, MI-E via face mask with the same pressure protocols as those used on day 1 was employed to investigate the effect of the interface (ETT vs face mask) on air flow (Figure 1c).

One cough cycle comprised 3 s of insufflation, 2 s of exsufflation, and 2 s of pause, with a total of 5 consecutive coughs (repetitions) within one set. All participants received a total of 5 sets per treatment session with a rest period of < 2 min between each set. Longer insufflation followed by shorter exsufflation and low inhale flow setting were chosen based on previous results from the lung-model analysis to simulate the physiology of a cough.[17-19] Further detailed information about the MI-E treatment protocol can be found in the supplementary material (available at http://www.rcjournal.com).

Measurements

The CoughAssist E70 (Phillips Respironics, Murrysville, Pennsylvania) was serially connected to a flow meter (CITREX H4 gas flow analyzer, IMT Analytics, Buchs, Switzerland), a single-use antibacterial filter, and either the ETT or face mask interface (Fig. 2). The flow meter was calibrated and validated annually by IMT Analytics, wherein the confirmed maximal uncertainty error was ≤ 0.75% for all measurements. Insufflation-exsufflation air flow was measured every 0.001 s during the entire treatment session. The primary outcome was PEF (in L/s): the lowest value of air flow measured during exsufflation since the value was measured and analyzed with negative signs (See e-Figure 2 of the supplementary material available at http://www.rcjournal.com).

The secondary outcomes were the feasibility and safety of MI-E therapy when using either ETT or face mask interface with pressures ranging from +30/−30 to +50/−50 cm H_2O. These outcomes were evaluated using the percentage of session completion and the number of adverse events that occurred during the application of MI-E therapy. Adverse events were defined as systolic blood pressure increase > 20%, mean arterial pressure decrease > 15% from baseline, HR ≥ 140 beats/min or increased by > 20% from baseline, S_{pO_2} < 85% even after oxygen administered for a maximum of 2 min, and frequency increase of > 50% from baseline and/or > 35 breaths/min. Participants were also asked to report any discomfort (eg, dyspnea, dizziness, nausea, worsening of gastro-oesophageal reflux, chest or abdominal discomfort) during or after MI-E therapy[4,15] and to report their satisfaction with the treatment using a 5-point Likert scale, from 1 = very dissatisfied to 5 = very satisfied, if they were able to respond to the questions (Richmond Agitation-Sedation Scale[20] score between −1 and +1). Simple chest radiographs were evaluated daily until the day after the completion of the MI-E therapy sessions to confirm that no complications, such as pneumothorax or pneumomediastinum, had occurred.[16]

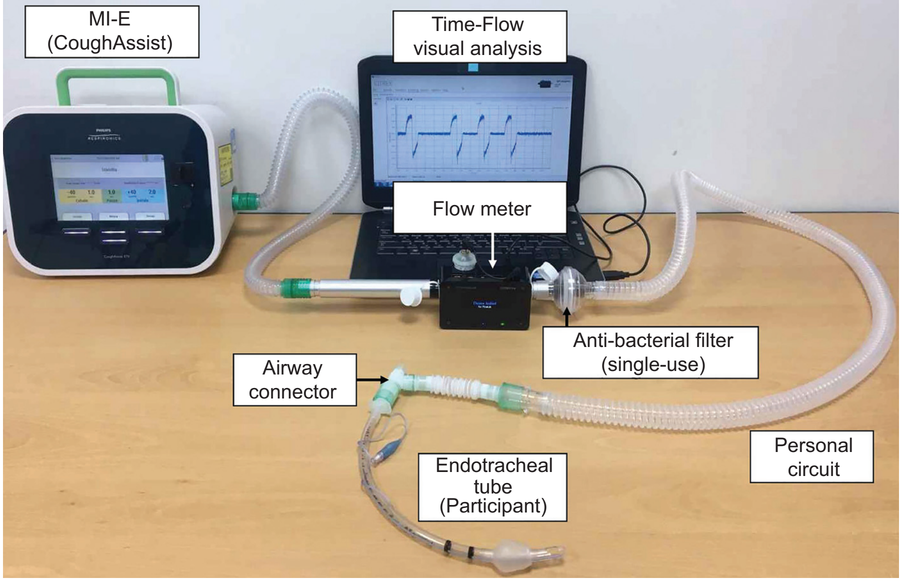

Fig. 2. Measurement of air flow during mechanical insufflation-exsufflation using a flow meter.

Information on demographic characteristics (age, sex, body mass index), reasons for ICU admission and admitted ICU type, severity of the current illness measured by the Acute Physiology and Chronic Health Evaluation score,[21] ETT internal diameter, and mechanical ventilation duration was obtained from medical records.

Statistical Analysis

As repeated measurements from the same participant were correlated with each other, a linear mixed-effect model was employed with PEF as the dependent variable.[22] The model included applied pressure, number of MI-E treatment sessions, number of coughs (repetitions) within each set, assigned group (group I or II), interface (ETT vs face mask), and any relevant interactions between a given pressure gradient and interface or number of sessions on PEF. The variabilities between participants, such as the absolute value of the baseline expiratory air flow, were included as random effects. Additionally, a generalized linear mixed model of binary logistic regression was applied to evaluate the variables related to sufficient exsufflation flow through MI-E treatment, defined as PEF < -2.7 L/s. The cutoff -2.7 L/s for PEF was chosen based on the study from Bach and Saporito,[23] which suggests that peak cough flow of 160 L/min (2.7 L/s), whether assisted or not, is the minimum expiratory air flow required to adequately clear secretions in subjects with artificial airways.[13,23] Other clinical and demographic characteristics were analyzed using descriptive statistics. Statistical analysis was performed using SPSS version 25 (IBM SPSS Statistics, IBM, Armonk, New York), and a $P < .05$ was considered statistically significant.

Results

Demographics of Participants

Of the 21 participants recruited, 2 (9.5%) were excluded because they could not cooperate with the insufflation-exsufflation cycle of MI-E therapy. That is, they could not coordinate their inspiration with 3 s of insufflation, and they coughed too early during this phase such that no air remained to effectively cough out during the exsufflation phase.

The remaining 19 participants completed the MI-E therapy via ETT. However, 3 participants (2 from group I and 1 from group II) discontinued additional MI-E treatment via face mask because they no longer had substantial secretions after extubation. Four participants (2 from group I and 2 from group II) could not receive MI-E therapy via face mask because their treatment plan for critical care was changed from extubation to tracheostomy owing to a high risk of post-extubation respiratory failure. A total of 12 participants (6 from each group) completed all the MI-E sessions with both ETT and face mask interfaces (See e-Figure 1 of the supplementary material available at http://www.rcjournal.com). The internal diameter of the ETT ranged from 6.5–8.0 mm. The participants' characteristics are presented in Table 1.

PEF Differences According to Interfaces: ETT Versus Face Mask

Adjusted mean PEF was calculated assuming that the covariables other than the pressure gradient (ie, number of treatment sessions, assigned group for pressure setting protocol, and number of coughs within a set) were fixed to the average values. For each pressure gradient, PEF via ETT was always slower than that generated via face mask (Table 2). Figure 3 shows that the PEF generated during MI-E became faster as a larger pressure gradient was applied whether via ETT or face mask. A comparison of the PEF according to the type of interface used, within the same participants, at each applied pressure is also provided in e-Figure 3 (supplementary materials available at http://www.rcjournal.com). When a pressure gradient of +40/−40 cm H_2O was applied, only 172 of 528 MI-E trials via ETT (32.6%) achieved a PEF faster than the −2.7 L/s cutoff, whereas 304 of 343 MI-E trials via face mask (88.6%) exceeded the PEF cutoff. Even at +50/−50 cm H_2O pressure gradient, 66 of 85 MI-E via ETT trials (77.6%) reached a PEF < −2.7 L/s, whereas 55 of 60 MI-E via face mask trials (91.7%) reached the cutoff.

Table 1. Characteristics of the Participants

Characteristics	Study Population (N = 12)
Age, y	74.0 ± 10.2
Gender	
Male	9 (75.0)
Female	3 (25.0)
BMI	21.1 ± 3.16
APACHE II at ICU admission	19.5 ± 9.35
ICU type	
Medical	3 (25.0)
Cardiovascular	7 (58.3)
Surgical	2 (16.7)
Main cause for ICU admission	
ARDS	5 (41.7)
After thoracic surgery	7 (58.3)
S_{pO_2}/F_{IO_2}, mm Hg	286.14 ± 76.73
PEEP, cm H_2O	5.42 ± 1.24
ETT size (mm); internal diameter	
6.5	1 (8.3)
7.0	4 (33.3)
7.5	6 (50.0)
8.0	1 (8.3)
Intubation period, d	6.83 ± 3.69

Data are presented as mean ± SD or n (%).
BMI = body mass index
APACHE = Acute Physiology and Chronic Health Evaluation
ETT = endotracheal tube.

Feasibility and Safety of MI-E Application through ETT

No adverse events with respect to hemodynamic instability were reported during or after the application of MI-E at all pressure stages to +50/−50 cm H_2O through both interfaces. Neither pneumothorax nor pneumomediastinum was reported from daily evaluation of simple chest radiographs during and after the MI-E treatment period. None of the participants rejected the completion of the incremental pressure protocols via both ETT and face mask. Among the 8 participants who were able to answer the questions, no treatment-related discomfort was reported; however, one participant reported nausea after MI-E through the ETT, which resolved within 5 min. Those 8 participants provided their responses for the Likert scale of satisfaction; average scores of 3.6 and 3.9 were reported for MI-E via ETT and face mask, respectively. When asked which interface they found more comfortable, 4 participants preferred ETT, 3 preferred face mask, and one considered both interfaces to be similarly comfortable.

Determinants of PEF During MI-E Use

The linear mixed-effect model analysis demonstrated that the interface (ETT vs face mask), pressure, and number of treatment sessions were factors associated with PEF (Table 3). Compared with PEF generated at +30/−30 cm H_2O, the increasing pressure gradient generated faster PEF (negative number of effect estimates for PEF difference represents faster velocity). Compared to face mask, MI-E through ETT resulted in slower PEF (positive number of effect estimates for PEF difference represents slower velocity). Furthermore, the interaction between interface type and pressure was also correlated with PEF (Table 3). Therefore, the absolute

Table 2. Comparison of Peak Expiratory Flow During Mechanical Insufflation-Exsufflation According to the Interfaces: Endotracheal Tube Versus Face Mask

Pressure (cm H_2O)	PEF via Endotracheal Tube (L/s)	PEF via Face Mask (L/s)
+30/−30	−2.18 (−2.37 to −1.99)	−2.66 (−2.85 to −2.47)
+30/−40	−2.37 (−2.56 to −2.18)	−3.00 (−3.18 to −2.81)
+40/−40	−2.52 (−2.70 to −2.34)	−3.11 (−3.29 to −2.94)
+40/−50	−2.73 (−2.92 to −2.54)	−3.33 (−3.52 to −3.14)
+50/−50	−2.96 (−3.15 to −2.77)	−3.36 (−3.55 to −3.18)

Numbers are adjusted mean PEF (95% CI).
Adjusted mean PEF was calculated using other covariables (number of treatment session, assigned group for pressure setting protocol, and number of coughs with a set) assumed to be fixed as constant average values.
PEF = peak expiratory flow

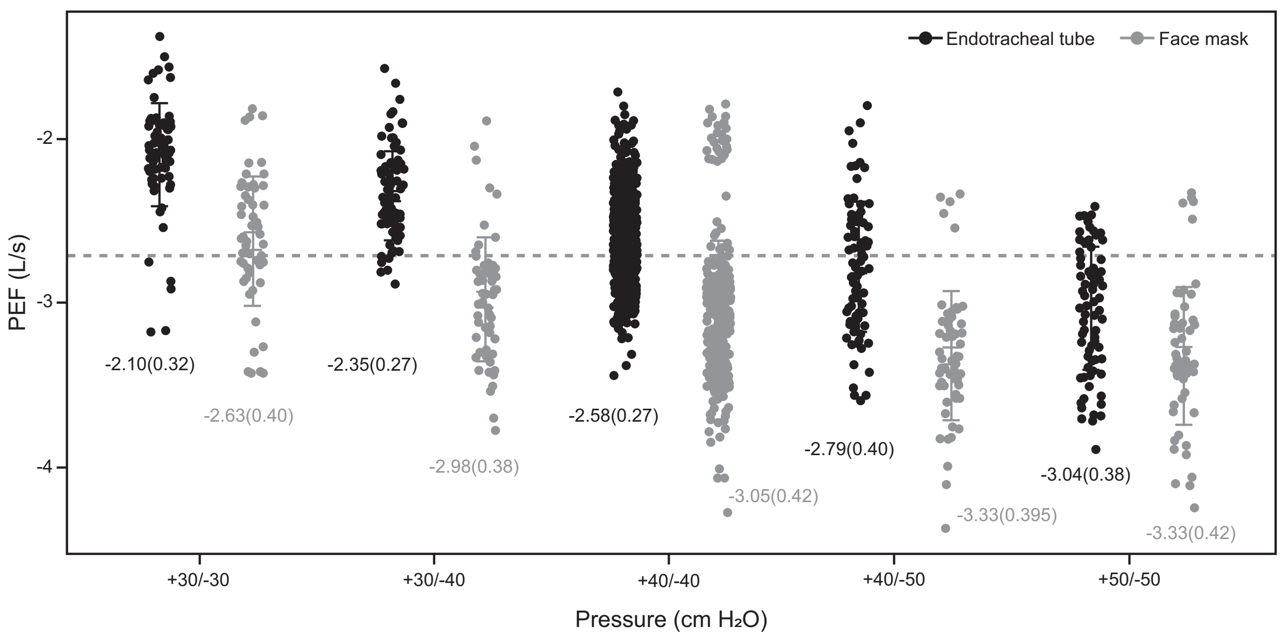

Fig. 3. Peak expiratory flow (PEF) during mechanical insufflation-exsufflation treatment according to pressure gradient and interface. Numbers represent mean (SD). Dashed line indicates −2.7 L/s cutoff.

Table 3. Linear Mixed-Effect Model Analysis for Peak Expiratory Flow

Predictor	*P*	Effect Estimates for PEF difference (L/s) (95% CI)
Pressure setting protocol (group I vs II)	.54	
Number of treatment sessions	< .001	
Repetitions within set	.057	
Pressure	< .001	+30/−30 cm H_2O (reference)
	+30/−40 cm H_2O	−0.37 (−0.58 to −0.15)†
	+40/−40 cm H_2O	−0.50 (−0.67 to −0.33)
	+40/−50 cm H_2O	−0.72 (−0.93 to −0.50)
	+50/−50 cm H_2O	−0.85 (−1.07 to −0.64)
	< .001	
Interface	Endotracheal tube	Face mask (reference)
		+0.48 (0.36–0.60)‡
Interaction		
Interface × Pressure	.02	
Number of treatment session × Pressure	< .001	

PEF = peak expiratory flow
† Negative number of effect estimate for PEF difference represents faster velocity.
‡ Positive number of effect estimate for PEF difference represents slower velocity.

amount of increase in the PEF owing to the increase in the pressure gradient varied depending on the interface. However, the assigned pressure setting protocol (group I or II) was not associated with the velocity of the PEF. In the analysis of the generalized linear mixed model, the factors related to whether PEF exceeded the cutoff −2.7 L/s were number of treatment sessions, interface (ETT vs face mask), and pressure—the same factors reported from the linear mixed-effect model analysis (Table 4).

Discussion

This study reveals that the PEF generated during MI-E treatment was influenced by the interface, pressure gradient, and number of treatment sessions. An ETT increases airway resistance since it is a long, narrow tube; therefore, the PEF through the ETT became slower in critically ill subjects on invasive mechanical ventilation. This may hamper the efficiency of sputum removal via

Table 4. Generalized Linear Mixed Model Analysis for Predicting Whether Peak Expiratory Flow Reaches 2.7 L/s

Predictor	*P*	Odds Ratio [95% CI]
Pressure setting protocol (group I vs II)	.72	
Number of treatment sessions	< .001	
Repetitions within set	.31	
Pressure	< .001	+30/−30 cm H_2O (reference)
	+30/−40 cm H_2O	5.856 (1.883–18.21)
	+40/−40 cm H_2O	58.43 (22.73–150.2)
	+40/−50 cm H_2O	187.0 (54.27–644.4)
	+50/−50 cm H_2O	862.9 (235.4–3,162)
Interface	< .001	Face mask (reference)
	Endotracheal tube	0.006 (0.003–0.014)

artificial airway; therefore, when applying MI-E through the ETT interface, a higher-pressure gradient of up to +50/−50 cm H_2O could be recommended to obtain a PEF equivalent to that when using the face mask interface.

Although several studies still selected a pressure of +40/−40 cm H_2O for MI-E through ETT,[3,24,25] more recent studies have reported the feasibility and safety of MI-E use via ETT with pressures up to +50/−50 cm H_2O.[10,11] Additionally, our study reported that a pressure of +50/−50 cm H_2O was more beneficial in generating faster PEF and was safe and feasible for intubated participants. These results are in line with previous bench studies with a lung model, which recommended pressure > +40/−40 or +50/−50 cm H_2O in subjects with artificial airways or higher airway resistance.[13,26]

Ventilator-induced lung injury (VILI) occurs when high lung volumes cause alveolar stretch injury and subsequent biologic and systemic reactions.[27] Since the plateau pressure is considered to be a variable that reflects the risk of lung overdistention,[28] either a low tidal volume or low plateau pressure is conventionally preferred to prevent VILI. On the other hand, there has been little evidence about inducing VILI from intermittent short durations of high peak inspiratory pressure, such as in MI-E treatment. Meanwhile, many studies that applied MI-E using an insufflation pressure of 50 cm H_2O reported improved lung conditions immediately after the treatment.[10,29] In terms of exsufflation, −50 cm H_2O is less negative pressure than that physiologically produced by a cough or negative pressure delivered through endotracheal suctioning (recommended as 95 to 200 cm H_2O).[30] Although the CoughAssist E70 can produce negative pressures of up to −70 cm H_2O, only pressures within −50 cm H_2O were used in this study following previously reported protocols[3,8-12] for participants admitted to the ICU. As shown in Table 2, when applying MI-E via ETT, even when using a pressure of +50/−50 cm H_2O, the PEF was still slower than when using a pressure of +40/−40 cm H_2O via face mask. For effective elimination of airway secretions, a negative pressure below −50 cm H_2O might be required. However, safety issues, such as atelectasis, when applying further negative pressure via ETT in patients receiving mechanical ventilation, especially with the PEEP setting, remain to be investigated.

By analyzing the physiology of a cough, a PEF 160–180 L/min has been proposed as the cutoff to achieve effective secretion elimination.[15,23,31-32] Therefore, a PEF 2.7 L/s was regarded as the goal of minimum PEF generation during MI-E therapy in this study (Table 4). Irrespective of such absolute PEF values or applied pressure, the expiratory flow bias,[19] that is, the difference in the absolute value of air flow regardless of the insufflation-exsufflation direction, has been suggested to be better correlated with the actual mucus displacement in a bench study simulating a patient with an artificial airway on mechanical ventilation.[19] In this study, the flow bias was larger with the ETT compared to the face mask (see e-Table 1 of the supplementary material available at http://www.rcjournal.com). If the flow bias rather than the PEF is regarded as the sole index of effective sputum removal, then it is possible to interpret that the MI-E treatment through an ETT could be performed with lower pressure than a face mask. However, in this case as well, the pressure setting of +50/−50 cm H_2O is still preferable with the ETT as the expiratory flow bias was steadily increasing up to +50/−50 cm H_2O; meanwhile, +40/−50 cm H_2O might be enough for the face mask since the flow bias decreased when the insufflation pressure was increased from +40/−50 cm H_2O to +50/−50 cm H_2O. Additionally, these results suggest that unlike the protocols utilized in the previous studies[9] it might be more appropriate to secure the insufflation volume[33] by increasing the insufflation time rather than the insufflation pressure because increasing the pressure increases the insufflation flow (flow = Δ pressure/resistance) and thus decreases the flow bias.

The result of a faster PEF with a face mask than an ETT in our study might be related not only with the applied interface but also with the different time points when the

MI-E was applied. Difference in the participants' sedation levels and cooperation, fewer secretions, and decreased airway resistance, which could change within the study period, might have influenced the generated PEF. In this study, however, the MI-E therapy sessions could only be provided first through ETT and next through face mask after extubation; a reversed order was not possible in clinical settings.

Another limitation of this study is the lack of information regarding the amount of airway secretions eliminated and the clinical benefits such as changes in S_{pO_2} levels or success of mechanical ventilation weaning after MI-E application, which should be considered in future studies. In addition, MI-E application strategies other than pressure gradients were not included in this study. For example, the insufflation time affects the insufflation-exsufflation volumes that might affect the PEF or expiratory flow bias and eventually the efficiency of sputum removal.[33,34] However, in this study, the insufflation time was fixed at 3 s. Lastly, limited sample size may have influenced the significance of interfaces on generated PEF; however, the post hoc power analysis indicated statistically enough power for this study based on a large number of repetitive measurements within the same participants. A sample size of 12, with a total of 1,500 measurements, was found to achieve 100%, 95%, and 92% power for the main effect of the interface, the main effect of the pressure, and their interaction effect, respectively. The minimum detectable difference was assumed to be 0.17 L/s (10 L/min)[34,35], and a subject variance and a residual variance were assumed to be 0.08 and 0.05, respectively, based on our study data.

MI-E through a tracheostomy tube was not evaluated, although 4 of the initially enrolled 21 subjects (19%) underwent tracheostomy after extubation. As MI-E can be successfully applied through the tracheostomy tube as well as the ETT,[6,23,24] future research should also include the tracheostomized population to expand the use of MI-E in critical care.

Conclusions

The use of MI-E via ETT generated slower PEF than did the use of MI-E via face mask, suggesting that a higher-pressure protocol should be considered for intubated patients. An insufflation-exsufflation pressure of +50/−50 cm H_2O was necessary to produce a high PEF faster than 2.7 L/s, and the applications were safe and feasible. The factors related to PEF generation by MI-E were pressure gradient, interface, and number of session repetitions.

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