Effects of Mechanical Insufflation-Exsufflation on Respiratory Parameters for Patients With Chronic Airway Secretion Encumbrance

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Effects of Mechanical Insufflation-Exsufflation on Respiratory Parameters for Patients With Chronic Airway Secretion Encumbrance*

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Study objectives: **To analyze the physiologic effects and tolerance of mechanical insufflation-exsufflation (MI-E) for patients with chronic ventilatory failure of various etiologies.**
Design: **Prospective clinical trial.**
Setting: **Rehabilitation unit of a university hospital.**
Patients or participants: **Thirteen patients with amyotrophic lateral sclerosis (ALS), 9 patients with severe COPD, and 7 patients with other neuromuscular disorders (oNMDs) with chronic airway secretion encumbrance and decreases in oxyhemoglobin saturation (Spo_2).**
Interventions: **Pressures of MI-E of 15 cm H_2O, 30 cm H_2O, and 40 cm H_2O were cycled to each patient, with 3 s for insufflation and 4 s for exsufflation. One application was six cycles at each pressure for a total of three applications.**
Measurements and results: **We continuously evaluated respiratory inductance plethysmography (RIP) and Spo_2 during every application. Peak cough flow (PCF) and dyspnea (Borg Scale) were also measured before the first and after the last application. The technique was well tolerated in all patient groups. Median Spo_2 improved significantly ($p < 0.005$) in all patient groups. Median PCF improved significantly ($p < 0.005$) in the ALS and oNMD groups from 170 to 200 L/min and from 180 to 220 L/min, respectively, and dyspnea improved significantly in the patients with oNMDs and patients with COPD from 3 to 1 and from 2 to 0.75, respectively. Breathing pattern characteristics (RIP) did not deteriorate after MI-E in any patient groups. Inspiratory flow limitation significantly decreased at the highest MI-E pressures for the ALS group.**
Conclusions: **Our results confirm good tolerance and physiologic improvement in patients with restrictive disease and in patients with obstructive disease, suggesting that MI-E may be a potential complement to noninvasive ventilation for a wide variety of patient groups.**
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Key words: amyotrophic lateral sclerosis; COPD; cough flow; mechanical insufflation-exsufflation; neuromuscular disorders; oxygen saturation; respiratory inductive plethysmography

Abbreviations: ALS = amyotrophic lateral sclerosis; IQR = interquartile range; MI-E = mechanical insufflation-exsufflation; MIP = maximal inspiratory pressure; NMD = neuromuscular disorder; NPPV = noninvasive positive pressure ventilation; oNMD = other neuromuscular disorder; PCF = peak cough flow; PEFMF = peak expiratory flow to mean expiratory flow ratio; PIFMF = peak inspiratory flow to mean inspiratory flow ratio; RIP = respiratory inductive plethysmography; Spo_2 = oxyhemoglobin saturation; $\dot{V}E$ = minute ventilation; VT = tidal volume

Individuals with neuromuscular disorders (NMDs) such as amyotrophic lateral sclerosis (ALS) and muscular dystrophy have an impaired cough and a reduction in peak cough flows (PCFs) as a result of inspiratory and expiratory muscle weakness.[1–3] Bulbar dysfunction results in the inability to control the glottis and maintain upper airway patency, further decreasing PCFs.[1] In pulmonary disorders such as chronic bronchitis and emphysema, the reduced expiratory flow resulting from dynamic airway compression and increased viscosity of bronchial secretions is probably the main cause of cough ineffectiveness.[2] Excessive secretions have also been

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considered a cause of failure of noninvasive positive pressure ventilation (NPPV) in acute exacerbations of COPD.[3]

Cough flows have value in predicting successful extubation and mortality rate in patients with neuromuscular disorders and COPD.[4,5] Cough augmentation with mechanical insufflation-exsufflation (MI-E) produces a significant increase in PCF and facilitates airway secretion clearance in NMDs.[6,7] It has been reported to be successful in avoiding hospitalizations, pneumonias, episodes of respiratory failure, and tracheotomy for patients with Duchenne muscular dystrophy,[8] spinal muscular atrophy,[9] and ALS.[1]

With regard to COPD, although earlier publications[10] described some benefit, Sivasothy et al[11] reported that MI-E decreased PCF and resulted in no subjective benefit, suggesting that it may even exacerbate hyperinflation. However, only low pressures were used in this study, and higher pressures were used in the more successful studies.[7,12] The aim of the present study was to evaluate the tolerance and effect of various pressure settings of MI-E on breathing pattern, PCF, and oxygen saturation for patients with COPD or NMDs.

Methods and Materials

Patients

Patients with severe COPD or NMDs were referred to our rehabilitation unit after at least one episode of acute respiratory failure. All who complained of chronic airway congestion and difficulty clearing airway secretions, had decreases in baseline oxyhemoglobin saturation (Spo_2), and provided consent satisfied the criteria for inclusion in this study. Exclusion criteria were medical instability, any changes in respiratory management during the 3 prior months, or need for any antibiotic therapy in the prior 4 weeks. From October 2002 to January 2003, 9 patients with severe COPD (COPD group), 13 patients with ALS (ALS group), and 7 patients with other NMDs (oNMDs) [oNMDs group] admitted for pulmonary rehabilitation were studied, and no referred patients were excluded. The diagnosis of COPD was made according to criteria established by the American Thoracic Society,[13] and NMDs were diagnosed in all patients by a neurologist who specialized in NMDs. No patients refused to participate in the study.

Four patients with COPD received long-term oxygen therapy and continued it during the study; one patient received NPPV, and three patients received both long-term oxygen therapy and NPPV. The ALS group included 10 patients with severe bulbar involvement; 11 patients with ALS received NPPV. The oNMD group included four patients with myotonic dystrophy, one patient with Duchenne muscular dystrophy, and two patients with other muscular dystrophies. Six of the seven patients received NPPV. Demographic data are shown in Table 1.

Measurements

Static lung volumes were measured by body plethysmographs (6200 Autobox DL; SensorMedics; Yorba Linda, CA), and dynamic lung volumes were measured by mass flow sensors (Vmax229; SensorMedics) with the patients in the seated position according to standard procedures.[14] The predicted values of Quanjer[15] were used. The inspiratory muscle strength was assessed by measuring maximal inspiratory pressure (MIP) at functional residual capacity according to the method of Black and Hyatt.[16] The highest of three attempts was recorded.

Spirometry, MIP, maximal expiratory pressure, and resting awake blood gases from radial artery samples (RapidLab 860; Ciba-Corning; Sudburry, England) were measured before the first application in the morning with the patient spontaneously breathing room air. Dyspnea and PCF were measured before the first and after the last application. Respiratory inductive plethysmography (RIP) was measured during all applications.

MI-E Settings

Mechanical cough assistance was provided by using the Cough-Assist device (JH Emerson Company; Cambridge, MA). The pressures are generated by a two-stage centrifugal blower. The positive and negative pressures may be set for insufflation and exsufflation, up to a maximum of 60 cm H_2O.[17] For each patient, each application was six insufflation-exsufflation cycles at each of the following pressures: 15 to – 15 cm H_2O, 30 to − 30 cm H_2O, and 40 to – 40 cm H_2O.

Table 1—*Patient Demographics

Demographics	oNMD (n = 7)	ALS (n = 13)	COPD (n = 9)
Age, yr	29 (26–49)	55 (47–68)	69 (54–73)
Male/female gender, No.	2/5	11/2	8/1
FEV_1, L	1.05 (0.61–2)	1.39 (0.89–2.30)	0.92 (0.53–1.28)
FEV_1 % predicted	55 (27–62)	54 (27–66)	34 (26–41)
FVC, L	1.26 (0.81–2.29)	1.91 (0.98–2.51)	1.83 (1.5–2.54)
FVC % predicted	55 (27–59)	51 (25–59)	61 (52–67)
FEV_1/FVC, %	88 (83–98)	85 (81–90)	48 (38–57)
$FEF_{25–75}$, L/s	0.96 (0.79–2.00)	1.78 (0.85–2.94)	0.32 (0.19–0.66)
$FEF_{25–75}$, %	35 (19–64)	47 (25–74)	11 (7–21)
MIP, cm H_2O	42.0 (33.6–57.3)	31.0 (22.0–52.0)	ND
MEP, cm H_2O	41.0 (23.0–59.0)	38.0 (20.0–51.0)	ND
Pao_2, mm Hg	77.6 (72–96.4)	83.7 (74.3–87.8)	59.9 (55.1–66.1)
$Paco_2$, mm Hg	43.0 (33.6–57.3)	40.4 (36.3–44.6)	50.7 (44.3–59.9)

*Data are expressed as median (IQR), unless otherwise indicated. $FEF_{25–75}$ = forced expiratory flow at 25 to 75% of FVC; MEP = maximal expiratory pressure; ND = not done.

The timing of the cycle was 3-s insufflation, 4-s exsufflation, and a postexsufflation 4-s pause. There was a 2-min rest period between each application, during which the RIP measurements were obtained. During exsufflation, ALS and oNMD patients were actively told to cough, while patients with COPD were advised to exhale slowly. After the sixth insufflation to 40 cm H_2O of the last application, the subjects were asked to cough forcefully on their own, as described by Barach et al.[18]

Quantitative RIP

RIP was recorded using the SomnoStar PT device (SensorMedics). The input leads for RIP consisted of two cloth belts that covered curved wires encircling the chest and abdomen. Initial calibration of the ribcage and abdominal signals were performed during the first 5 min of operation using a qualitative diagnostic calibration procedure.[19] A software program (RespiEvents version 4.2e; SensorMedics) allowed the calculation of breathing pattern parameters, including tidal volume (VT), minute ventilation ($\dot{V}E$), peak inspiratory flow to mean inspiratory flow ratio (PIFMF), and the peak expiratory flow to mean expiratory flow ratio (PEFMF). The latter parameters are considered to detect flow limitation, with values > 1.5 representing normal (rounded) RIP-derived waveforms. As the flow waveform flattens, indicating increased resistance, the values approach 1.0. Spo_2, also included in the SomnoStar PT and analyzed by the same software, was evaluated simultaneously.

For each patient, measurements of VT, $\dot{V}E$, PIFMF, PEFMF, and Spo_2 were performed during 2 min in the supine position at baseline and 1 min after each MI-E application. Median values for each parameter were analyzed.

PCF were measured before the first application and after the last application by having the patient cough as forcibly as possible through a peak flowmeter (Assess; Health Scan Products; Cedar Grove, NJ). The maximum observed flows in four or five attempts were recorded.[7] For evaluating the effect of treatment on dyspnea, a Borg scale (0 = not at all breathless; 10 = maximal breathlessness) was administered before and after the intervention.[20]

Statistical Analysis

Statistical analysis was carried out using SPSS 10.0 (SPSS; Chicago, IL). Results are expressed as median and interquartile range (IQR). Comparisons between patient groups were done using the Mann-Whitney *U* test and differences between baseline and MI-E settings were compared using the Wilcoxon rank test. A Spearman rank correlation coefficient was used to examine the relationship between physiologic data; $p \leq 0.05$ was considered significant.

Results

The oNMD patient group was significantly younger than the ALS and COPD groups ($p = 0.024$ and $p = 0.004$, respectively) [Table 1]. Pao_2 was significantly lower in the COPD group compared to the oNMD and ALS groups ($p = 0.016$ and $p = 0.001$, respectively). $Paco_2$ values were significantly higher and the FEV_1 significantly lower in the COPD group compared to the ALS group ($p = 0.003$ and $p = 0.0023$, respectively). PCF at baseline was not significantly different between patient groups. In the ALS group, there was a significant positive correlation between PCF (at baseline and after MI-E) and MIP ($r = 0.637$, $p = 0.035$, and $r = 0.778$, $p = 0.005$, respectively), and a negative correlation between baseline VT and $Paco_2$ ($r = -0.852$, $p = 0.0015$).

There were no significant differences between groups in VT, $\dot{V}E$, PIFMF, PEFMF, and Spo_2 at baseline. In patients with NMD, only PCF improved significantly after MI-E (180 L/min vs 220 L/min); in patients with COPD, Spo_2 improved significantly only after 40 to -40 cm H_2O of MI-E (92% vs 97%). In patients with ALS, both PCF and Spo_2 improved significantly after 40 to -40 cm H_2O. Moreover, in this group PIFMF increased significantly between 15 to -15 cm H_2O, 30 to -30 cm H_2O, and 40 to -40 cm H_2O (1.38 vs 1.45 and 1.38 vs 1.44). Although there was no significant difference for the rest of breathing pattern parameters during different settings for each patient group, after MI-E at 30 to -30 cm H_2O, PIFMF was significantly lower in patients with COPD, compared to ALS (1.36 vs 1.44, $p = 0.046$).

Dyspnea (Borg scale) improved significantly after 40 to -40 cm H_2O of MI-E in patients with COPD and patients with NMDs. Pulmonary parameters as a function of MI-E settings and significant comparisons are reported in Table 2.

In patients with COPD, we did not find any significant correlation between severity of obstruction (FEV_1) and impairment of breathing pattern during MI-E (measured by VT, $\dot{V}E$, PIFMF, and PEFMF). In patients with ALS, we did find a positive correlation between FVC and MIP with PCF after MI-E ($r = 0.720$, $p = 0.008$, and $r = 0.778$, $p = 0.005$, respectively). The effects of MI-E on the RIP measurements of VT, $\dot{V}E$, and Spo_2 are shown in Figure 1. No patients complained of abdominal distension or vomiting, blood-streaked sputum, chest pain, discomfort, nor had any other symptoms or signs suggestive of barotrauma at any time during or following the study.

Discussion

MI-E was well tolerated, and it significantly improved PCF and Spo_2 for patients with NMD and COPD with airway secretion encumbrance, especially when used at pressures of 40 to -40 cm H_2O. It has been demonstrated in Rhesus monkeys that these pressures result in the greatest expiratory flows and result in no airway damage.[21] While some patients find MI-E to be most effective at pressures of ≥ 60 cm H_2O, the great majority of patients in clinical practice receive it at 40 to -40 cm H_2O.

Table 2—*Pulmonary Parameters and Dyspnea Scores as a Function of MI-E Applications

Variables	NMD (n = 7)	ALS (n = 13)	COPD (n = 9)
Baseline			
PCF, L/min	180 (150–275)	170 (128–300)	250 (173–288)
Spo_2, %	94 (92–96)	94 (94–95)	92 (91–94)
Dyspnea (Borg)	2.0 (0.4–3.3)	2.0 (0.8–3.5)	3.0 (2.0–4.0)
VT, mL	468 (390–808)	408 (338–604)	366 (340–484)
$\dot{V}E$, L/min	12.7 (6.4–20.5)	8.5 (6.6–11.5)	8.0 (6.6–11.1)
PIFMF	1.45 (1.39–1.59)	1.38 (1.35–1.43)	1.36 (1.34–1.46)
PEFMF	1.55 (1.50–1.78)	1.54 (1.42–1.60)	1.58 (1.44–1.67)
After MI-E 15 cm H_2O			
PCF, L/min	ND	ND	ND
Spo_2, %	96 (92–98)	95 (93–97)	95 (92–95)
Dyspnea (Borg)	ND	ND	ND
VT, mL	460 (416–708)	390 (341–454)	428 (358–506)
$\dot{V}E$, L/min	11.4 (6.4–13.7)	8.9 (7.0–11.1)	8.4 (5.9–11.2)
PIFMF	1.47 (1.42–1.48)	1.45 (1.34–1.54)†	1.37 (1.32–1.48)
PEFMF	1.54 (1.48–1.63)	1.51 (1.41–1.57)	1.64 (1.39–1.77)
After MI-E 30 cm H_2O			
PCF, L/min	ND	ND	ND
Spo_2, %	95 (93.5–97.0)	95.0 (94.0–97.0)	95.0 (91.5–95.0)
Dyspnea (Borg)	ND	ND	ND
VT, mL	440 (416–664)	408 (348–467)	404 (328–488)
$\dot{V}E$, L/min	10.4 (8.2–16.5)	9.8 (7.7–10.4)	8.2 (6.2–10.6)
PIFMF	1.43 (1.40–1.56)	1.44 (1.38–1.50)†‖	1.36 (1.30–1.43)‖
PEFMF	1.55 (1.43–1.71)	1.54 (1.50–1.56)	1.50 (1.44–1.73)
After MI-E 40 cm H_2O			
PCF, L/min	220 (190–300)†	200 (170–352)‡	275 (195–315)
Spo_2, %	98 (97–98)‡	98 (97–98)‡	97 (95–97)§
Dyspnea (Borg)	0.75 (0–2.3)†	1.0 (0.5–2.0)	1.0 (1.0–2.5)§
VT, mL	588 (446–764)	494 (389–576)	440 (346–558)
$\dot{V}E$, L/min	11.4 (9.5–14.7)	10.6 (8.6–17.8)	9.5 (5.3–10.2)
PIFMF	1.40 (1.39–1.54)	1.43 (1.37–1.52)	1.36 (1.33–1.45)
PEFMF	1.52 (1.47–1.67)	1.54 (1.51–1.56)	1.60 (1.42–1.76)

*Data are expressed as median (IQR). See Table 1 for expansion of abbreviation.
†$p < 0.05$ compared to baseline.
‡$p < 0.005$ compared to baseline.
§$p < 0.02$ compared to baseline.
‖$p < 0.05$, ALS vs COPD.

Thus, these are the widely preferred pressures in clinical practice for both comfort and effectiveness in many hundreds of patients and thousands of applications in patients with neuromuscular weakness over the last 50 years.[22] Likewise, Barach and Beck[23] wrote that the pulmonary pressure changes generated by MI-E are a small fraction of those generated by respiratory muscle contractions during a normal cough. Thus, it is not surprising that there was no apparent barotrauma nor other respiratory complications in this study.

Breathing pattern characteristics did not deteriorate after MI-E. This is consistent with studies that reported significant increases in vital capacity and Spo_2 when using MI-E to clear airway secretions.[6,7,10] In a study[6] including patients with NMD, FEV_1 following MI-E only increased, demonstrating no persistent airway collapse or air-trapping. The present study demonstrated that the same could be true for MI-E used in COPD when evaluating breathing parameters by RIP.

The increase in Spo_2 with MI-E was not associated with other changes in RIP parameters. It is possible that the benefit of the technique, improving the recruitment of nonventilated pulmonary zones, and removing mucous debris, attains a more evident improvement in gas exchange rather than in breathing pattern. However, to answer this question it would have been necessary to examine the effects of MI-E on ventilation perfusion ratio distribution and oxygen and carbon dioxide exchange, which was beyond the aim of our study.

RIP is the most widely accepted method for quantitative and qualitative noninvasive respiratory measurements, and has been demonstrated to accurately measure VT,[24,25] and detect inspiratory and expiratory flow limitation or collapse.[26,27] The former occurs because of the narrowing or collapse of the

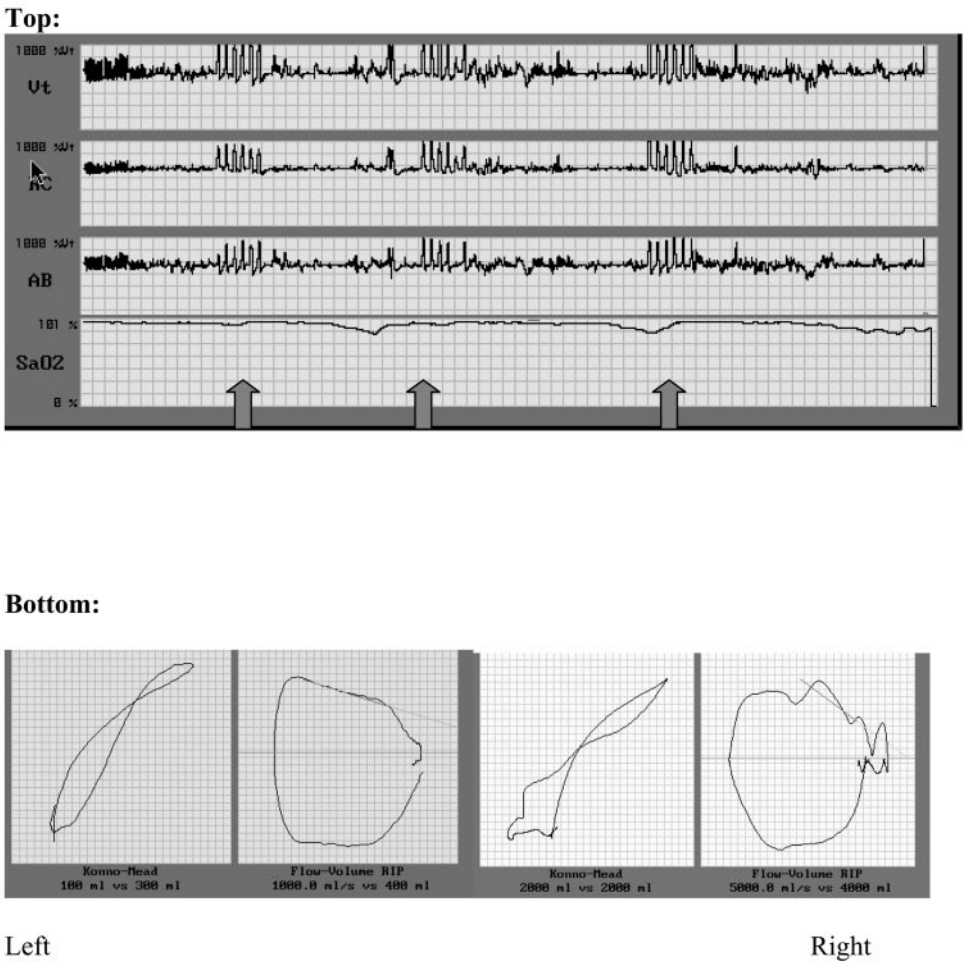

FIGURE 1. RIP measurements of VT, and Spo_2 in a patient with ALS during MI-E (AC = rib cage signals, AB = abdominal signals). *Top*: RIP signals show significant VT and respiratory rate increase as well as rise of Spo_2 during different settings of MI-E (arrows). *Bottom*: Using breath-by-breath analysis of PIFMF and PEFMF during baseline (*left*) and after MI-E at 40 to – 40 cm H_2O (*right*), it was possible to evaluate effects on airflow limitation.

upper airway in response to the negative intrathoracic pressure during inspiration. Clinically this is seen in patients with sleep-disordered breathing,[28] and during negative-pressure ventilatory support.[29] Application of negative pressure (− 5 cm H_2O) at the mouth during resting tidal respiration has been shown to enhance detection of expiratory flow limitation.[30]

In our study, we used RIP to evaluate the effect of MI-E. In the oNMD group, we did not find any deterioration in breathing pattern or pulmonary parameters. In the ALS group, PIFMF even significantly increased with pressures at 40 to − 40 cm H_2O, suggesting decreased pharyngeal resistance.[27] In the COPD group, the shape of flow volume waveforms were also little affected by MI-E, and median PEFMF remained constant over all the MI-E applications (Table 2). Therefore, concerns by Sivasothy et al[11] that MI-E may exacerbate hyperinflation do not appear to be justified with these measurements. However, evaluation of lung volumes should be considered for more accurate conclusions.

In patients with ALS, the majority with bulbar involvement and receiving domiciliary NPPV, a significant improvement in PCF and progressive increase of Spo_2 with increasing MI-E pressures was demonstrated. No subjects complained of discomfort during MI-E, and the patients with COPD actually reported relief of dyspnea (Borg scale). This is consistent with other published experiences in > 2,000 applications of MI-E, the majority of which were in patients with intrinsic lung disease.[10]

Although we cannot exclude a placebo effect, the significant improvement in Spo_2 at the end of the last application suggested that they indeed benefited. In fact, contrary to the findings of Sivasothy el al,[11]

we did not find deterioration of PCF with MI-E. The differences found might be attributed to the technique of PCF measurements (pneumotachograph in the study by Sivasothy et al,[11] and a standard peak flowmeter in our study), coughs performed without the exsufflation, and the significantly higher MI-E pressures used in our study. The use of lower pressures may be ineffective, as is suggested by the improvement in Spo_2 in patients with COPD (as well as in other patient groups) being reached only at the highest pressure application. In fact, Gomez-Merino et al,[31] using MI-E connected to a lung model, found that insufflation and exsufflation pressures of 35 to − 35 cm H_2O or 40 to − 40 cm H_2O were the most effective in achieving higher values of PCF, and these pressures are also those suggested by the manufacturer.[17] These authors[31] observed that because the minimally clinically effective cough flow of 2.7 L/s was not achieved at insufflation-exsufflation spans of < 30 cm H_2O, settings below 30 to − 30 cm H_2O should not be expected to be effective. Moreover, this technique can be applied in a more aggressive protocol, for longer periods of time to obtain adequate PCFs to prevent mucus plugging and profuse airway secretions, especially during respiratory tract infections and acute respiratory failure.[32,33]

Conclusion

This prospective study confirms that MI-E can improve PCF and oxygenation in ALS and other NMDs. In patients with COPD, it improved oxygenation and breathlessness without a significant improvement in PCF, but also without any deterioration in breathing pattern or pulmonary parameters. Taken together, these findings suggest that MI-E may be a potential complement to noninvasive ventilation for a wide variety of patient groups, and may help to reduce the frequency of pulmonary complications caused by retention of secretions.

The results of this study may indicate the use of MI-E for secretion management during ventilator weaning[5] and possibly for COPD exacerbations with excessive secretions.[34] Further validation is warranted in a larger patient population.

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