Physiologic Benefits of Mechanical Insufflation-Exsufflation in Children With Neuromuscular Diseases*

Brigitte Fauroux, MD, PhD; Nathalie Guillemot, MD; Guillaume Aubertin, MD; Nadia Nathan, MD; Agathe Labit, MD; Annick Clément, MD, PhD; and Frédéric Lofaso, MD, PhD

Study objectives: To analyze the physiologic effects and tolerance of mechanical insufflation-exsufflation (MI-E) by means of mechanical cough assistance (Cough Assist; JH Emerson Company; Cambridge, MA) for children with neuromuscular disease.
Design: Prospective clinical trial.
Setting: Physiology laboratory of a pediatric pulmonary department of a university hospital.
Patients: Seventeen children with Duchenne muscular dystrophy (n = 4), spinal muscular atrophy (n = 4), or other congenital myopathy (n = 9) who were in a stable state.
Interventions: Pressures of 15, 30, and 40 cm H_2O were cycled to each patient, with 2 s for insufflation and 3 s for exsufflation. One application consisted of six cycles at each pressure for a total of three applications.
Measurements and results: Airway pressure and airflow were measured during every application. Breathing pattern, vital capacity (VC), sniff nasal inspiratory pressure (SNIP), peak expiratory flow (PEF), and respiratory comfort were evaluated at baseline and after each application. The tolerance of the patients was excellent, with a significant increase in the respiratory comfort score in all of the patients (p = 0.02). Expired volume during the MI-E application increased significantly to reach twice the VC at 40 cm H_2O. Mean and maximal inspiratory and expiratory flows increased in a pressure-dependent manner. Breathing pattern did not change after the MI-E applications and pulse oximetric saturation remained stable within normal values, but the mean end-tidal carbon dioxide pressure decreased significantly. VC did not change, but the mean SNIP and PEF improved significantly after MI-E applications.
Conclusions: Our results confirm the good tolerance and physiologic short-term benefit of the MI-E in children with neuromuscular disease who were in a stable state.
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Key words: Duchenne muscular dystrophy; gas exchange; lung function; mechanical insufflation-exsufflation; myopathy; physiotherapy; respiratory mechanics; spinal muscular atrophy

Abbreviations: fr = respiratory rate; IPPB = intermittent positive-pressure breathing; MI-E = mechanical insufflation-exsufflation; Paw = airway pressure; PCF = peak cough flow; PEF = peak expiratory flow; P_{ETCO_2} = end-tidal carbon dioxide pressure; SNIP = sniff nasal inspiratory pressure; SpO_2 = pulse oximetric saturation; VAS = visual analog scale; VC = vital capacity; V_E = minute ventilation; Vexp = expired volume measured during the mechanical insufflation-exsufflation; V_T = tidal volume

Patients with neuromuscular disease demonstrate significant abnormalities in chest wall and lung mechanics, which are attributed to ventilatory muscle weakness. The reduction of chest wall compliance is explained by the inability to fully expand and empty the chest, which leads to stiffening of the joints and tissues of the rib cage. The reduction of lung compliance is explained by atelectasis resulting from breathing at low lung volume and from the inability to clear the airways of secretion by an effective cough. In 1972, intermittent positive-pressure breathing (IPPB) for 5 min to induce lung hyperinflation was reported to increase dynamic lung compliance by up to 70% for at least 3 h in patients with kyphoscoliosis.[1]

More than 30 years later, the same intervention was shown to induce a moderate, short-term, but significant increase in lung compliance in patients with amyotrophic lateral sclerosis.[2] Vital capacity (VC) improved immediately after IPPB in patients with acute quadriparesis.[3] However, earlier studies[4,5] of IPPB in patients with neuromuscular disorders showed no effect on lung volumes or compliance. IPPB has also been used to improve cough performance, and a synergic effect of IPPB and standard physiotherapy on peak cough flow (PCF) has been demonstrated in neuromuscular patients.[6]

An alternative to IPPB and its possible beneficial effects is mechanical insufflation-exsufflation (MI-E) through a face mask using a mechanical cough assistance device called the Cough Assist (JH Emerson Company; Cambridge, MA). As IPPB, this device uses positive pressure during the inspiration to promote maximal lung inflation. Furthermore, this inflation is followed by an abrupt switch to negative pressure to the upper airway, thereby simulating a normal cough. When this device has assisted the cough of children and adults who have various neuromuscular diseases, it generated a higher PCF than unassisted cough and other classic assisted cough methods.[7] MI-E has been also demonstrated to improve other baseline respiratory parameters like pulse oximetric saturation (SpO$_2$), as well as dyspnea in adult patients with COPD, amyotrophic lateral sclerosis, and other neuromuscular disease.[8]

All these beneficial effects suggest that MI-E can be used preventively in populations at risk of respiratory complications and who need assistance for airway clearance. However, it is unclear how to set the pressures, particularly in children, who represent an important population that may benefit from this technique. We therefore decided to perform a physiologic study to help the clinician to optimize the different settings, in particular the inspiratory and expiratory pressures. In practice, the aim of the study was to determine the effects of a step-by-step increase in insufflation-exsufflation levels on the tolerance, the expired volume, which is an important determinant of cough performance,[6] the breathing pattern, and the respiratory function just after this lung and chest mobilization. Because of the greater difficulty to perform a physiologic study in an acute situation in children, we took the option to start with a study in patients who were in a stable state.

Materials and Methods

Patients

The patients were recruited on a consecutive basis from our outpatient clinic and were included in the study as follows: (1) if they had a documented neuromuscular disease that had been diagnosed by a pediatric neurologist specializing in neuromuscular disease; (2) if they had been clinically stable for at least 1 month; (3) if they were able to perform respiratory muscle tests and use the visual analog respiratory comfort scale; and (4) they had been accepted to participate to the study. All of the patients were naïve to MI-E but had received routine IPPB at home. All the patients and their parents gave their informed consent.

Measurements

All of the measurements and the protocol were performed on the same afternoon, with the patients having gone through their daily physiotherapy session in the morning.

Respiratory Muscle Function and Respiratory Comfort

Before and after each of the three MI-E sessions, all of the patients were asked to perform at least three physician-accepted VC curves, and the curves with the highest VC were used for the final analysis.[9] Results were expressed as absolute values and as the predicted percentage of published values, with height calculated as the arm span.[10,11] Patients were also asked to perform three PCF and three peak expiratory flow (PEF) maneuvers; the best value of the combined PCF and PEF maneuvers were retained for analysis and expressed in absolute values and as the percent predicted.[12] Thereafter, patients were asked to perform at least five short, sharp maximal sniffs, with the most negative value being retained for analysis.[13,14] A mean ($\pm$ SD) value of 104 $\pm$ 26 cm H$_2$O in boys and 93 $\pm$ 23 cm H$_2$O in girls is considered normal for the sniff nasal inspiratory pressure (SNIP) maneuver.[15] Respiratory sensation was also evaluated by means of a visual analog scale (VAS). The patients rated their respiratory comfort on an interval scale that was a 10-cm horizontal line with the words "I breathe very badly" and "I breathe very well" on the left side and right side, respectively. The patients were instructed to place a vertical mark on the line such that its position relative to the two extremes indicated the magnitude of

*From the Assistance Publique-Hôpitaux de Paris (Drs. Fauroux, Guillemot, Aubertin, Nathan, Labit, and Clément), Hôpital Armand Trousseau, Pediatric Pulmonary Department, Paris, France; and Assistance Publique-Hôpitaux de Paris (Dr. Lofaso), Hôpital Raymond Poincaré, Université de Versailles Saint Quentin en Yvelines, Department of Clinical Physiology, Garches, France and Institut National de la Santé et de la Recherche Médicale U 851, Créteil, France.
Correspondence to: Brigitte Fauroux, MD, PhD, AP-HP, Hôpital Armand Trousseau, Pediatric Pulmonary Department, Research unit INSERM UMR-S 719, Université Pierre et Marie Curie-Paris 6, 28 Ave du Docteur Arnold Netter, Paris, F-75012 France; e-mail: brigitte.fauroux@trs.aphp.fr
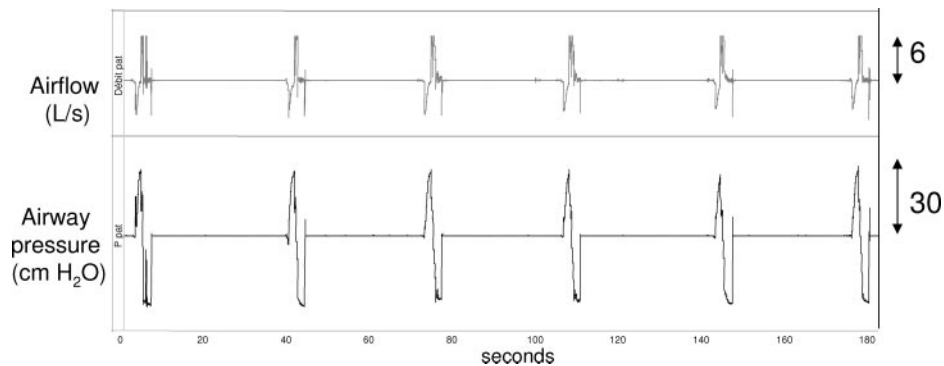
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FIGURE 1. Tracing of a patient during the MI-E with an inspiratory pressure set at 40 cm H_2O and an expiratory pressure set at $-$ 40 cm H_2O. Note that the Paw never exceeded 35 cm H_2O.

their comfort at the moment of the assessment. The comfort score was expressed in millimeters (from 0 to 100 mm) and was the distance of the mark from the left-hand side of the VAS.[16]

Breathing Pattern

During the spontaneous breathing recordings, the patients breathed through a mouthpiece with a nose clip. Airflow, measured by a pneumotachograph (model No. 3; Fleisch; Lausanne, Switzerland), and airway pressure (Paw), measured by a differential pressure transducer ($\pm$ 100 cm H_2O, model MP 45; Validyne; Northridge, CA) were mounted directly on the mouthpiece. End-tidal carbon dioxide pressure (PETCO_2) was sampled at the mouthpiece with an infrared analyzer (Ultracap; Nellcor Puritan-Bennett; Courtaboeuf, France). SpO_2 was recorded continuously by pulse oximetry (Ultracap; Nellcor Puritan-Bennett). During the MI-E sessions, the pneumotachograph and the pressure transducer were inserted between the face mask and the ventilatory circuit.

All the signals were digitized at 128 Hz and sampled for analysis using an analogic/numeric acquisition system (MP 100; Biopac Systems; Goleta, CA), run on a personal computer (Elonex; Gennevilliers, France) with appropriate software (Acknowledge; Acknowledge Software; East Palo Alto, CA). Breathing pattern was determined from flow tracings. Tidal volume (VT) was calculated by integrating the airflow during inspiration. Minute ventilation (VE) was calculated by multiplying VT by respiratory rate (fr).

MI-E Settings

Mechanical cough assistance was provided by using the Cough Assist device (JH Emerson Company). 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. For each patient, three MI-E sessions were performed. Each session comprised six insufflation-exsufflation cycles. For each session, the inspiratory-expiratory pressures were + 15 to $-$ 15 cm H_2O, + 30 to $-$ 30 cm H_2O, and + 40 to $-$ 40 cm H_2O, as evaluated previously in an study of adult patients.[8] The timing of the cycle was 2 s of insufflation, then 3 s of exsufflation. There was a 30-s rest period between each application (Fig 1). Patients were instructed to let the device make them inhale fully during inspiration, and to exhale fully during expiration. The interface was the recommended face mask, which was firmly placed on the patient's face during the MI-E applications.

Paw and airflow were recorded continuously during the MI-E sessions. The volume measured during the MI-E was the expiratory volume (Vexp), considering that lung inflation started at functional residual capacity and that exsufflation finished below functional residual capacity. The breathing pattern, with the recording of airflow, PETCO_2, and SpO_2, was recorded for 2 min before the first level of MI-E application and for 1 min after each MI-E application. Respiratory comfort and respiratory muscle function were evaluated immediately afterward.

Statistical Analysis

The data are given as the mean $\pm$ SD. Repeated-measures analysis of variance was used for testing if the three MI-E applications had a significant effect on the different variables. When analysis of variance appears appropriate (F test with $p < 0.05$), pairwise comparisons were performed using the Fisher least comparison test. A p value of < 0.05 was considered to be the limit of significance.

Table 1—Characteristics of the Patients*

| Characteristics | Gender | | Age, yr | Weight, kg | Able to Walk, No. | NPPV, No. |
	Boy	Girl				
Duchenne muscular dystrophy (n = 4)	4	0	15 ± 3	36 ± 22	1	3
Spinal muscular atrophy (n = 4)	2	2	8 ± 3	16 ± 3	1	2
Other neuromuscular disease (n = 9)	6	3	10 ± 2	38 ± 17	2	5
Total population (n = 17)	12	5	11 ± 4	33 ± 18	4	10

*Values are given as the mean $\pm$ SD, unless otherwise indicated. NPPV = noninvasive positive pressure ventilation.

Table 2—*Breathing Pattern and Respiratory Muscle Function at Baseline in the Three Groups of Patients**

Variables	Duchenne Muscular Dystrophy (n = 4)	Spinal Muscular Atrophy (n = 4)	Other Myopathies (n = 9)
Breathing pattern			
V_T, L	0.31 ± 0.10	0.16 ± 0.04	0.30 ± 0.11
fr, breaths/min	21 ± 2	33 ± 18	25 ± 8
$\dot{V}_E$, L/min	6.5 ± 2.3	4.9 ± 1.7	6.9 ± 1.7
Gas exchange			
SpO_2, %	97.5 ± 1.0	94.9 ± 2.6	97.8 ± 1.6
$PETCO_2$, mm Hg	39.7 ± 3.2	36.6 ± 5.0	41.5 ± 2.8
Respiratory muscle function			
VC			
L	1.33 ± 0.95	0.39 ± 0.29	1.26 ± 1.39
% predicted	36 ± 40	25 ± 38	67 ± 26
SNIP			
cm H_2O	25 ± 21	22 ± 21	34 ± 17
% predicted	21 ± 28	23 ± 22	36 ± 24
PEF or PCF, L/min	210 ± 108	67 ± 108	180 ± 87
PEF, % predicted	49 ± 36	30 ± 28	65 ± 48
Respiratory comfort, VAS/100	71 ± 29	64 ± 20	78 ± 19

*Values are given as the mean ± SD, unless otherwise indicated.

RESULTS

Characteristics of the Patients

Seventeen consecutive patients participated to the study, and none of the patients who was proposed for the study refused participation. The characteristics of the patients are presented in Table 1. One of the nine patients with another neuromuscular disease had a merosin deficit, one had spina bifida, and the other seven patients had an unknown myopathy. The age of the patients ranged from 5 to 18 years, with the patients having spinal muscular atrophy being the youngest. Thir-teen patients were wheelchair bound, and 10 patients received long-term noninvasive positive-pressure ventilation at home.

At baseline, the mean SpO_2 and mean $PETCO_2$ were within the normal range, at the expense of a certain degree of rapid, shallow breathing with a low V_T and a high fr (mean fr, 26 ± 11 breaths/min) [Table 2]. All of the patients had significant respiratory muscle weakness with a mean VC of 1.04 ± 1.13 L and a mean SNIP of 29 ± 19 cm H_2O. The patients with spinal muscular atrophy, who were the youngest group, had the lowest PEF or PCF, as well as the lowest respiratory comfort.
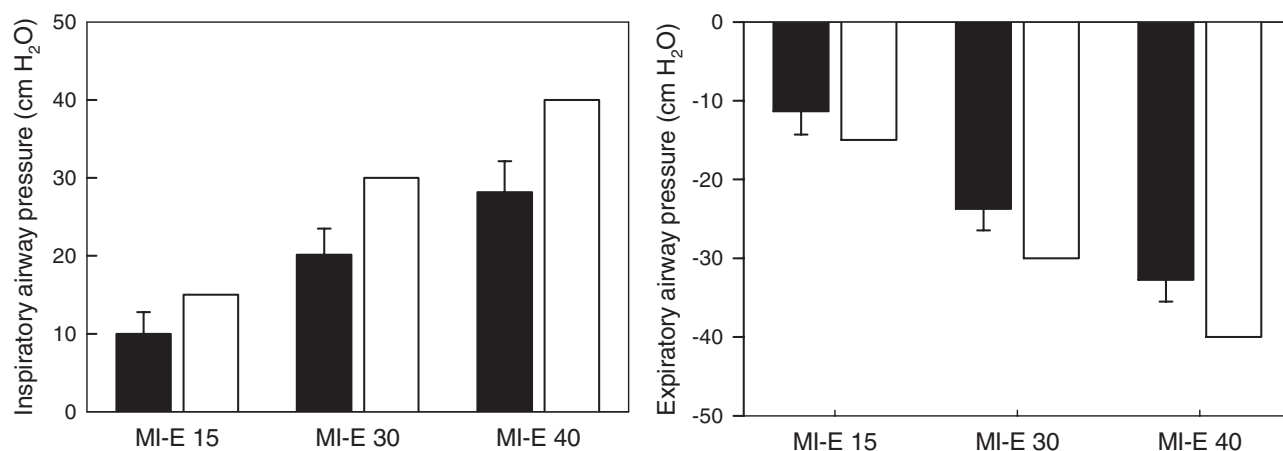

FIGURE 2. Difference between the Paw set on the MI-E (white bars) and the Paw measured during the MI-E applications (black bars) at three pressure levels (15 cm H_2O [MI-E 15], 30 cm H_2O [MI-E 30], and 40 cm H_2O [MI-E 40]).
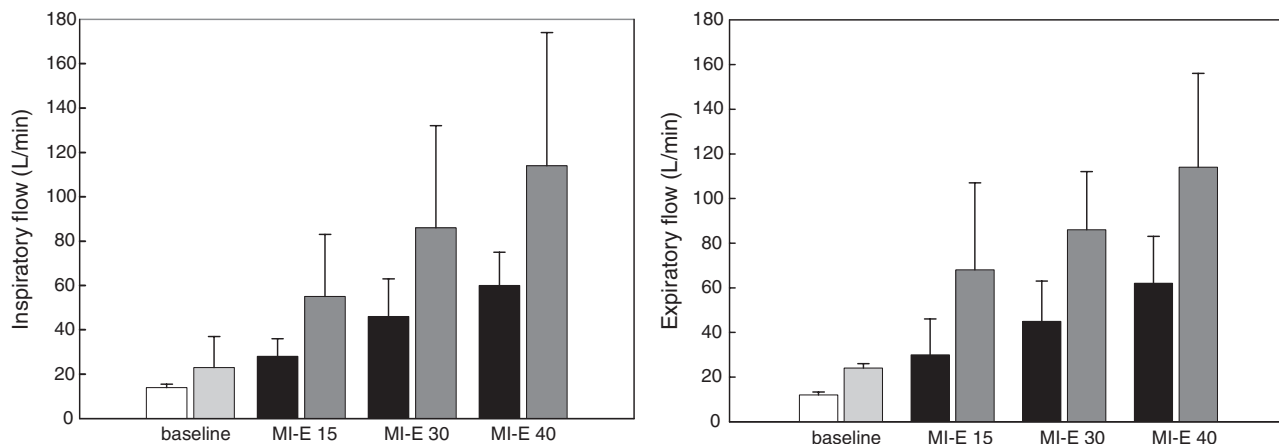
FIGURE 3. Mean (black bars) and maximal (dark gray bars) inspiratory and expiratory flows during the MI-E applications at the three pressure levels (15, 30, and 40 cm H_2O). Mean (white bars) and maximal (light gray bars) inspiratory and expiratory flows during spontaneous breathing are given for comparison. See the legend of Figure 2 for abbreviations not used in the text.

One patient with Duchenne muscular dystrophy did not perform the SNIP maneuver after the 40 cm H_2O MI-E session because of a mild epistaxis, due to the plug used for the SNIP maneuver. However, he performed the other tests.

Performance of the MI-E

The Paw measured on the facial mask during the MI-E applications were constantly lower than the inspiratory and expiratory pressures set on the device (Fig 2). A pressure-dependent increase in the maximal and mean inspiratory and expiratory flows was observed during the three MI-E applications (Fig 3). This translated into a proportional increase in Vexp

FIGURE 4. Mean Vexp during the MI-E applications at the three pressure levels (15, 30, and 40 cm H_2O; black bars). Mean baseline values of VT (white bar) and VC (gray bar) are given for comparison. See the legend of Figure 2 for abbreviations not used in the text.

during the MI-E maneuver (Fig 4). Of note, the mean Vexp during the 40 cm H_2O application (1.87 ± 1.04 L) reached almost twice the mean VC of the population (1.04 ± 1.13 L).

Effect of the MI-E on the Breathing Pattern and Respiratory Muscle Efficiency

The MI-E had no significant effect of the breathing pattern and VC measured after each series of six applications (Table 3). SpO_2 remained stable within the normal range, but a significant decrease in $PETCO_2$ was observed after the 15-cm H_2O MI-E application (Table 3). This improvement in $PETCO_2$ persisted after the two other MI-E applications. A significant increase in the mean SNIP and the mean best PEF or PCF was also observed after the 40-cm H_2O MI-E application (Table 3). Individual data for the patients are shown in Figure 5. Most interestingly, a significant increase in the respiratory comfort was observed after the 40-cm H_2O MI-E application in all of the patients (Table 3).

Tolerance and Clinical Efficacy

The tolerance of the MI-E applications was excellent. No patients complained of abdominal distension, gastroesophageal reflux, or chest pain or discomfort, or had any other symptoms suggestive of barotrauma at any time during or after the study.
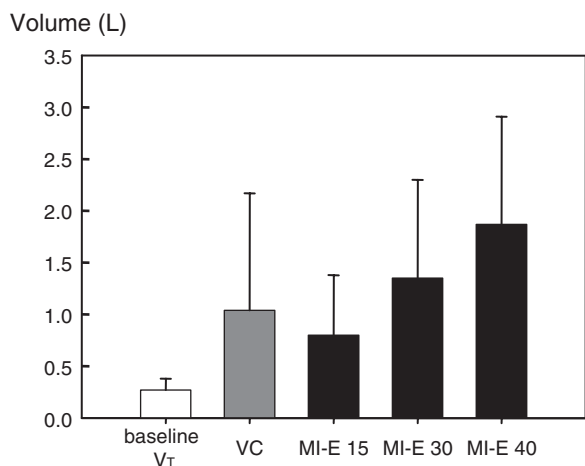
DISCUSSION

This study shows the good tolerance and the short-term physiologic benefits of one MI-E ses-

Table 3—Evolution of Breathing Pattern, Gas Exchange, and Respiratory Muscle Function After the MI-E Sessions With 15, 30, and 40 cm H_2O*

Variables	Baseline	After MI-E 15 cm H_2O	After MI-E 30 cm H_2O	After MI-E 40 cm H_2O	p Value†
Breathing pattern					
VT, L	0.27 ± 0.11	0.27 ± 0.13	0.27 ± 0.16	0.28 ± 0.15	NS
fr, breaths/min	26 ± 11	27 ± 12	26 ± 11	26 ± 10	NS
V̇E, L/min	6.3 ± 1.9	5.9 ± 1.5	6.2 ± 2.1	6.3 ± 1.7	NS
Gas exchange					
Spo$_2$, %	97.1 ± 2.1	96.6 ± 2.6	96.5 ± 2.2	96.4 ± 2.3	NS
Petco$_2$, mm Hg	39.9 ± 3.8	38.0 ± 4.4	37.7 ± 4.6	37.8 ± 4.7	< 0.0003
Respiratory muscle function					
VC, L	1.04 ± 1.13	1.01 ± 1.05	1.00 ± 0.99	1.04 ± 1.06	NS
SNIP,‡ cm H_2O	29 ± 19	30 ± 19	28 ± 18	31 ± 20	0.046
PEF or PCF, L/min	162 ± 97	173 ± 112	170 ± 102	192 ± 99	0.02
Respiratory comfort, VAS/100	73 ± 21	75 ± 18	76 ± 24	83 ± 19	0.02

*Values are given as the mean ± SD, unless otherwise indicated. NS = not significant.
†Analysis of variance.
‡Analysis of variance was performed in 16 patients.

sion in a group of young children with neuromuscular disease who were in a stable state. During the MI-E applications, a pressure-dependent increase in the mean and maximal inspiratory and expiratory pressures and flows was observed, which was associated with a parallel increase in Vexp. This improvement in alveolar ventilation translated into a significant decrease in Petco$_2$. Also, the 40-cm H_2O MI-E application was associated with a significant improvement in respiratory muscle efficiency in ballistic conditions (*ie*, requiring a quick maximal maneuver), as assessed by the SNIP and the PEF or PCF. Most interest-

ingly, respiratory comfort, quoted by the patients themselves, improved significantly after the 40-cm H_2O MI-E application.

This physiologic study demonstrates the efficacy of the MI-E to increase Vexp above VC. Vexp during the insufflation-exsufflation increased proportionally to the pressure swing to reach a volume as high as twice the mean VC at the highest level of pressure swing (1.87 ± 1.04 L). Also, during the exsufflation, a mean PEF of 114 ± 84 L/min could be generated. Because our patients were not solicited to cough or to produce a forced expiration during mechanical exsufflation, PEF did not
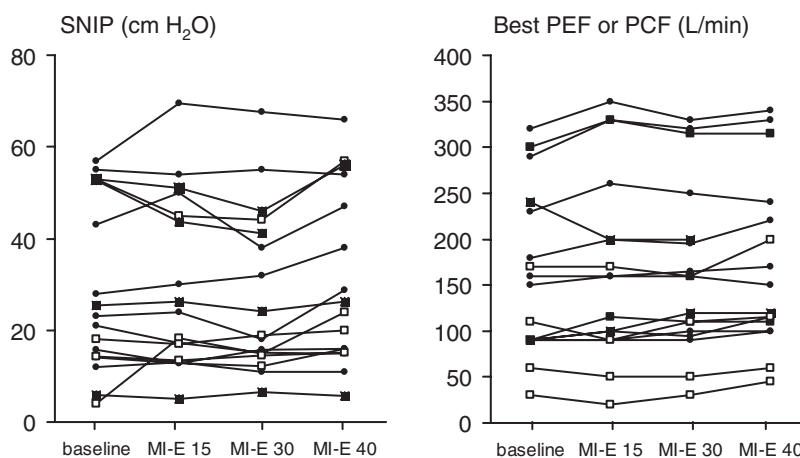

FIGURE 5. Individual data of the SNIP and the best PEF or PCF of the patients at baseline and after the MI-E applications at the three pressure levels (15, 30, and 40 cm H_2O). The patients with Duchenne muscular dystrophy, spinal muscular atrophy and other neuromuscular diseases are represented by the black squares, the open squares and the black dots, respectively. See the legend of Figure 2 for abbreviations not used in the text.

166

Original Research

reach the patient's volitional PCF. But, we are confident about the possible synergic effect of MI-E and volitional cough in these patients as it has been demonstrated by Chatwin et al.[7] The normal PCF in adults exceeds 360 L/min, and airway clearance is compromised at a PCF of < 160 L/min.[17,18] The limits for efficient PCF have not been validated for young children, but it is possible that thresholds may be lower in young children.

Winck et al[8] observed a significant improvement in PCF after MI-E in adults with neuromuscular diseases. We observed similar improvements in PCF in the patients included in the present study. In addition, we also tested SNIP and VC in order to better appreciate the influence of MI-E on the respiratory muscle output. We observed also an improvement in SNIP, but, curiously, VC did not change. A training effect may be excluded because all of the patients included in the present study were totally familiarized with the different respiratory muscle tests, which they performed routinely during their follow-up.[13] Respiratory muscle fatigue could have influenced the results. However, this does not seem to be the case, as documented by the global individual improvement of SNIP and the best PEF or PCF seen in Table 3 and Figure 5. SNIP values and the best PEF or PCF values deteriorated only in one patient with Duchenne muscular dystrophy, due to a mild epistaxis. The difference observed between SNIP and VC may be explained by the type of maneuver. Indeed, sniff and cough are generated during a rapid, ballistic maneuver, during which the respiratory muscles shorten at high speed, whereas the VC maneuver is a slower maneuver corresponding to the quietness of spontaneous breathing. Patients with neuromuscular disorders are not used to performing rapid motions of the respiratory system, as do, for example, health subjects during exercise. With the MI-E, they were solicited to abruptly change their respiratory system volume. These rapid changes in lung volume occurring during the MI-E simulate large and sharp inspiratory and cough maneuvers. Consequently, one can hypothesize that SNIP and cough maneuvers are better performed by neuromuscular disease patients after a short time of conditioning with MI-E. Thus, our hypothesis is that the MI-E, by "inflating" and "deflating" the lung quite quickly several times (six times in the present study at every pressure level), simulates a cough maneuver and as such "trains" the patient for a rapid inspiratory maneuver (ie, SNIP) and expiratory maneuver (ie, PEF or PCF). Rather than a real increase in respiratory muscle strength, which seems unlikely over such a short period, the MI-E enables the patient to reproduce and improve a rapid respiratory

maneuver. Obviously, in clinical practice, the cough maneuver rehabilitation is the most important.

VC is also an indicator of lung and chest wall compliance. In earlier studies, IPPB improved lung compliance and the work of breathing for up to 3 h in patients with kyphoscoliosis[1] or amyotrophic lateral sclerosis.[2] However, in adults with chronic neuromuscular disorders comparable to those our pediatric population, IPPB had no significant short-term benefit on chest wall or lung compliance.[4,5] Interestingly, VC improved immediately after IPPB in patients with acute quadriparesis[3]; however, the mean increase in VC was only 43 mL, which was statistically significant but was considered to be clinically irrelevant by the authors. In agreement with earlier studies[4,5] that did not find a significant immediate beneficial effect of mechanical insufflation on VC, lung compliance, and chest wall compliance, we did not observe any significant effect of MI-E on VC in our population.

As has been demonstrated with IPPB,[19] MI-E passively increased alveolar ventilation. As a result, $PETCO_2$ decreased during the minute that followed each MI-E application. The lack of improvement in SpO_2 may be explained by the normal values at baseline, leaving no room for improvement in this group of patients who were in a stable state. The patients were in a stable state, which thus precluded the evaluation of the MI-E effect on the improvement of airway secretion encumbrance.

Clearly, in the pairwise comparison with baseline values, the 40-cm H_2O MI-E was the only setting associated with improvements in SNIP, PEF or PCF, and respiratory comfort, whereas an improvement in $PETCO_2$ was already significant after the 15-cm H_2O application. The 40-cm H_2O setting was well tolerated by all of the patients. None of the patients complained of abdominal or chest discomfort, and no complication, such as gastroesophageal reflux, pneumothorax, or alveolar hemorrhage, was observed. Most importantly, respiratory comfort, identified by the patients themselves on a VAS, improved when higher pressures were used, with a statistically significant improvement noted only after the 40-cm H_2O application. This excellent tolerance has also been reported in a long-term observational study,[20] which included 62 patients with neuromuscular disease, aged 3 months to 28 years. The median duration of use was 13.4 months (range, 0.5 to 45.5 months). Complications did not occur, but two patients complained of abdominal pain and chest discomfort. Interestingly, chronic atelectasis resolved in four patients after MI-E therapy, and five patients experienced a reduction in the frequency of pneumonia.

The patient's cooperation is absolutely required for success using a device such as the MI-E device (ie,

the Cough Assist device). Indeed, the patient must allow the device to insufflate and thus to increase lung volume. Its efficacy is likely to be compromised in noncooperative children. The ability to close the glottis is also a necessary component for an efficient cough maneuver. This was not a problem in our group of patients, but patients with amyotrophic lateral sclerosis, who frequently have bulbar involvement, may not benefit from MI-E maneuvers.[21]

We acknowledge that our study has some limitations. All of the patients received routine IPPB at home, but they were naïve to MI-E. Respiratory comfort improved after the 40-cm H_2O MI-E was performed. However, we cannot exclude a placebo effect, with the subjects perceiving a bigger breath to be more therapeutic although not necessarily more comfortable, or a learning effect, considering that for the present study we took the option of applying a progressive increase in pressure, as had been performed by Winck et al,[8] who studied the MI-E in three groups of adult patients. We kept the same protocol with the three consecutive pressure levels, but we adapted the breathing pattern to young children. Indeed, the patients' mean fr was 26 ± 11 breaths/min. For this reason, the inspiratory time was set at 2 s and the expiratory time at 3 s. These settings were kept constant during the protocol. It is possible that the optimal settings of inspiratory and expiratory time may vary for the different patients, and for an individual patient according to their status (ie, stable or not). Further studies are warranted to verify this point. Finally, the relatively small number of patients included in the present study did not allow an analysis according to the underlying disease or the severity of respiratory muscle weakness. Further studies, including a larger number of patients, are clearly needed to validate our clinical observation that the MI-E may be associated with a larger benefit in patients having greater respiratory muscle impairment. In conclusion, our study shows the excellent tolerance and the short-term physiologic benefits in terms of improvement in CO_2 clearance and ballistic respiratory muscle performance in a group of young patients with neuromuscular disease who were in a stable state.

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