Respiration

Clinical Investigations

Respiration 2023;102:341–350
DOI: 10.1159/000529166

Received: October 11, 2022
Accepted: January 9, 2023
Published online: February 1, 2023

Home Use of Mechanical Insufflation/Exsufflation in Adult Patients in Western Switzerland

Georgia Mitropoulou[a] Raphael Heinzer[a, b] Jean-Paul Janssens[c]
Christophe von Garnier[a] Maura Prella[a]

[a]Division of Pulmonology, Department of Medicine, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland; [b]Center for Investigation and Research in Sleep, Department of Medicine, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland; [c]Division of Pulmonary Diseases, Department of Medicine, Geneva University Hospitals, Geneva, Switzerland

Keywords
Cough · Cough assistance · Mechanical insufflation-exsufflation · Neurological disease · Neuromuscular disease

Abstract
Background: Mechanical insufflation/exsufflation (MI-E) devices are often prescribed to patients with inefficient cough and recurrent infections, but their use in the home setting is not well characterized. ***Objective:*** The objective of this study was to report a real-life experience and identify factors that are associated with home MI-E use in adult patients. ***Methods:*** This is a cross-sectional observational study of adult subjects with neurological disease using MI-E at home for more than 3 months. ***Results:*** A total of 43 patients were included. Median age (interquartile range) was 48 (31–64) years. The most common diagnosis was muscular dystrophy (n = 15), followed by multiple sclerosis (n = 7) and amyotrophic lateral sclerosis (n = 7). 24 subjects (56%) reported using the MI-E at least once weekly. Based on device data downloads, the median objective use was 23% of days analysed (approximately 2 times per week). The vast majority (94%) of all participants reported using the device at least daily during an infectious episode, while 62% reported having used the device in emergency situations such as bronchoaspiration. Reported use correlated well with objective use (r = 0.82). Most subjects reported an improvement in their respiratory health (64%) and were satisfied with the device (78%). Higher reported and objective use were associated with increased symptoms (p = 0.001) and higher satisfaction with the device (p = 0.008). We found no association between frequency of use and baseline cough peak flow (CPF), bulbar impairment, non-invasive ventilation use, living environment, or supervised administration. ***Conclusion:*** Regular home MI-E use was associated with greater symptom burden and overall satisfaction with the device and was not influenced by baseline CPF. Patients without substantial bronchorrhea might not use the MI-E regularly but might still need to use the device at home during acute events. Therefore, familiarity with the MI-E via appropriate and repeated practical training is crucial.

Preliminary results were presented by G. Mitropoulou at the ERS conference on Respiratory failure and mechanical ventilation conference, 13-15.02.20, Berlin.
The study was performed at the Division of Pulmonology, Reference Centre for Neuromuscular Disorders, Lausanne University Hospital, Lausanne, Switzerland.

Karger@karger.com
www.karger.com/res

Correspondence to:
Georgia Mitropoulou, georgia.mitropoulou@chuv.ch

Introduction

Respiratory complications constitute the main cause of morbidity and mortality among patients with neurological disease. Acute airway obstruction due to mucus plugs can lead to acute respiratory failure and even death, while excessive secretions predispose to recurrent lower respiratory tract infections, progressive lung damage, and decreased quality of life. The role of cough augmentation techniques early in the disease process is important in preventing respiratory complications. Mechanical insufflation/exsufflation (MI-E) is an instrumental cough augmentation technique, which enhances the inspiratory and expiratory component of cough, resulting in an increased MI-E-assisted exsufflation flow [1–10]. Mechanical in-exsufflators were first developed in the 1950s [11–13] from modified conventional tank respirators. The use of MI-E regained popularity in the USA in the late 1980s as an adjunct to non-invasive ventilation (NIV). It was used to improve bronchial drainage and dyspnoea [7] and to avoid hospitalization and respiratory failure, leading to invasive ventilation and tracheostomy following chest infection in patients with Duchenne muscular dystrophy [14], spinal muscular atrophy [15], and amyotrophic lateral sclerosis (ALS, without bulbar involvement) [16]. MI-E devices became available in the UK, Europe, and Canada in the early 2000s and were shown to improve respiratory outcomes in adult and paediatric patients with diverse neurological or neuromuscular (NM) diseases [17–24]. MI-E together with NIV prevented the need for reintubation in subjects with NM disease after weaning from invasive mechanical ventilation [25, 26] and was deemed more effective and more tolerable than tracheal suctioning in tracheotomised patients with ALS [27]. Qualitative studies on the home use of MI-E devices have shown health and lifestyle benefits [22, 28, 29]. However, MI-E remains a costly treatment, and its implementation requires repeated interventions by trained professionals to ensure adequate training of patients and their caregivers [30, 31].

Current guidelines [32–38] propose the use of MI-E in case of unassisted cough peak flow (CPF) < 270 L/min and/or if manual cough augmentation techniques cannot achieve an appropriate bronchial drainage, particularly during chest infections. However, little information is available on long-term home MI-E use. Data from a cohort of heterogeneous NM patients in the UK [39] showed a median use of 60% of days analysed, while 22% of subjects used the device less than 10% of the days downloaded.

Given the significance of effective bronchial drainage in patients with neurological disease and the highly variable long-term usage rates of MI-E devices at home [39], it is important to obtain an accurate picture of clinical practice, treatment adherence as well as patient's priorities, all of which could help clinicians decide when and how to prescribe an MI-E. The aims of our study were to describe the characteristics of adult patients with a long-term MI-E prescription in Western Switzerland, provide information on device settings and self-reported and objective patterns of use, and report patients' perception of the treatment.

Methods

Participants

In this cross-sectional observational study, we included adult subjects with neurological disease, who had an MI-E at home for more than 3 months. Participants were recruited from two university hospitals (Lausanne University Hospital [CHUV] and Geneva University Hospitals [HUG]), as well as from regional hospitals and from pulmonologists in private practice in the western (French speaking) part of Switzerland, from September 2019 to May 2020. Subjects with tracheostomy were excluded from the study due to small sample size ($n = 2$).

Socioeconomic Data

Following recruitment and consent, a survey was used to collect information on socioeconomic data, in particular with regards to current living conditions and the presence of caregivers.

Clinical Information

Underlying neurological diagnosis, the presence or absence of cognitive impairment, and the degree of bulbar dysfunction upon inclusion were recorded for all subjects. The latter was assessed using the items "Speech" and "Swallowing" of the ALSFRS-r score on a 0–8 scale [40]. Bulbar impairment was rated as absent (ALSFRS-r score = 8), moderate (ALSFRS-r score ≥ 3 or ≤ 7), or severe (ALSFRS-r score ≤ 2) [41]. Pulmonary function tests and CPF at the time of MI-E initiation were documented, as well as current need for NIV, oxygen therapy, and use of other instrumental methods of cough augmentation. The subjects were asked to report current respiratory symptoms (cough, bronchial congestion, bronchorrhea) using an unstructured questionnaire.

MI-E Settings

CoughAssist E70™ (Philips Respironics, 1001 Murry Ridge Lane, Murrysville, PA 15668, USA) was the only device used in our population. CoughAssist E70™ settings were collected via Secure Data (SD) card and the dedicated software (DirectView, Philips Respironics). Pressure, time, flow, and oscillation settings had been titrated manually in order to allow or enhance secretion clearance while taking into account the patient's comfort and tolerance. Training for MI-E use had been provided at home by experienced physiotherapists or specialized respiratory nurses who also ensured follow-up, consisting of at least annual review of settings and instruction on MI-E use.

MI-E Use

In Switzerland, a CPF lower than 270 L/min constitutes a necessary condition for cost reimbursement of MI-E [36]. MI-E is proposed to all patients with inefficient cough for (a) the management of acute episodes, such as during a chest infection or bronchoaspiration and (b) in the case of chronically increased secretions, as a preventive measure that should be employed regularly to avoid respiratory complications.

Based on the above, upon prescription, the patients had received instructions with regards to the recommended frequency of use, on a case-by-case basis. Information on written usage recommendations was collected when available. Subjects were asked to report the frequency of MI-E use when not exacerbated by choosing one of the 6 following options: never, rarely, once or twice per month, once a week, 2 to 3 times per week, more than 4 times per week. Regular use was defined as MI-E use at least 2 to 3 times per week. Participants were also asked to describe the frequency of MI-E use during exacerbations. Information on administration (self-administration, administration by non-professional caregivers or by trained healthcare professionals) was collected. A Likert scale was used to assess the perceived value of the treatment, and participants were invited to comment on the positive and negative aspects related to its use. A translated version of the questionnaire is shown in online supplementary Table S1 (for all online suppl. material, see www.karger.com/doi/10.1159/000529166).

CoughAssist E70™ use data were collected via SD card and were analysed using the dedicated software (DirectView, Philips Respironics). Objective treatment adherence was assessed by the percentage of days used over the last 12 months or since MI-E prescription, if less than 12 months.

Statistical Analysis

Statistical analysis was performed using version 13 of STATA software (StataCorp LLC, Texas, TX, USA). Reported use was expressed either as an ordinal variable based on the six options in the survey or as a dichotomized variable (regular use being defined as reported use at least twice weekly). Objective use was defined as the percentage of days used according to data downloads. Associations between categorical variables were tested using Fisher's exact test, with a two-sided p value <0.05. Associations between dichotomized variables and quantitative variables were tested using the Wilcoxon-Mann-Whitney U test. Associations between categorical and continuous variables were assessed using the Kruskal-Wallis equality of population rank test and the Spearman regression coefficient. Missing data were not replaced.

Results

Subject Characteristics

We screened 64 patients who had an MI-E at home for more than 3 months. Of those, 2 patients with tracheostomy were excluded, 11 could not be contacted, and 8 refused to participate in the study or did not return the questionnaires and the MI-E SD card. Forty-three adult subjects (26 male, 17 female) with neurological disease were included in the study. Median (interquartile range)

Table 1. Subjects' characteristics

Characteristic	Result
Median age, year (IQR)	48 (31.5–64)
Gender, *n* (%)	
Female	17 (39.5)
Male	26 (60.5)
Institutionalized, *n* (%)	11 (26)
Age of institutionalized subjects, year (IQR)	69 (48.5–71.5)
Diagnosis, *n* (%)	
Muscular dystrophy	15 (34.8)
Duchenne muscular dystrophy	6 (13.9)
Facioscapulohumeral muscular dystrophy	2 (4.7)
Myotonic dystrophy	2 (4.7)
Emery-Dreifuss muscular dystrophy	1 (2.3)
Congenital muscular dystrophy (rigid spine syndrome)	1 (2.3)
Congenital muscular dystrophy	2 (4.7)
Limb-girdle muscular dystrophy	1 (2.3)
Amyotrophic lateral sclerosis	7 (16.3)
Spinal muscular atrophy type 2	4 (9.3)
Metabolic myopathies	2 (4.7)
Mucopolysaccharidosis type 2	1 (2.3)
Wilson's disease	1 (2.3)
Multiple sclerosis	7 (16.3)
Other diagnoses	8 (18.6)
Perinatal hypoxic-ischaemic encephalopathy	2 (4.7)
Spinal cord injury	2 (4.7)
Mitochondrial myopathy	1 (2.3)
Multiple system atrophy	1 (2.3)
Corticobasal degeneration	1 (2.3)
Lance-Adams syndrome (chronic post-hypoxic myoclonus)	1 (2.3)
NIV, *n* (%)	29 (67.4)
Long-term oxygen therapy, *n* (%)	2 (4.7)
Bulbar impairment[a], *n* (%)	
Absence	10 (23.3)
Mild/moderate	20 (46.5)
Severe	13 (30.2)
Cognitive impairment, *n* (%)	9 (20.9)
Baseline FVC, % of predicted value (IQR)	42 (25–53)
Baseline FEV_1, % of predicted value (IQR)	45 (28–54)
Baseline CPF[b] L/min (IQR)	120 (100–155)
Cough[c]	15 (35)
Bronchial congestion[c]	16 (37)
Bronchorrhea[c], *n* (%)	19 (44.1)

Baseline, at the time of MI-E initiation; CPF, unassisted cough peak flow; FCV, forced vital capacity; FEV_1, forced expiratory volume in 1st second; IQR, interquartile range. [a] Bulbar impairment was rated as absent (ALSFRS-r score = 8), mild/moderate (ALSFRS-r score ≥3 or ≤7), or severe (ALSFRS-r score ≤2) with the use of the items "Speech" and "Swallowing" of the ALSFRS-r score, on a 0–8 scale [40]. It was rated at inclusion. [b] CPF could not be measured in 9 subjects due to severe weakness. [c] Cough, bronchial congestion, or bronchorrhea were self-reported symptoms.

Table 2. Details on MI-E initiation, training, and administration

Median duration of MI-E use, months (IQR)	26 (15–60)
Elective initiation, *n* (%)	26 (74.2)
Initiation during an episode of chest infection, *n* (%)	9 (25.7)
Number of persons trained per participant, *n* (range)	2 (1–4)
MI-E administration by healthcare professionals, *n* (%)	25 (58.1)
MI-E administration by non-professionals (family/carer) only, *n* (%)	14 (32.6)
Self-administration only	2 (4.7)
Use of additional instrumental airway clearance technique[a]	12 (27.9)

MI-E, mechanical insufflation/exsufflation device; IQR, interquartile range. [a] In most cases of additional instrumental airway clearance technique, the subject used a device providing high frequency percussive ventilation.

Table 3. MI-E settings (values reported as *n* (%) or median [IQR])

Manual mode, *n* (%)	2 (5)
Automatic mode, *n* (%)*	37 (95)
Automated inspiratory trigger (Cough Trak™)	24 (65)
Insufflation pressure, cmH_2O (IQR)	25 (21.5–30)
Exsufflation pressure, cmH_2O (IQR)	−40 [(−30)–(−45)]
Insufflation time, s (IQR)	2 (1.6–2.2)
Exsufflation time, s (IQR)	2.5 (2–3)
Inspiratory flow profile, *n* (%)	
Low	4 (10)
Medium	28 (70)
High	8 (20)
Use of oscillations, *n* (%)	18 (45)
During insufflation only	1 (5.5)
During exsufflation only	7 (39)
During both insufflation and exsufflation	10 (55.5)

All patients used the CoughAssist E70™ device (Philips Respironics, 1001 Murry Ridge Lane, Murrysville, PA 15668, USA) with a mask interface. MI-E, mechanical insufflation/exsufflation device; IQR, interquartile range. * In all cases, settings were titrated initially using the manual mode before switching to the automatic mode to facilitate home use.

age was 48 (31–64) years. The most common diagnostic group was muscular dystrophy ($n = 15$), followed by multiple sclerosis (MS, $n = 7$) and ALS ($n = 7$).

Upon inclusion, severe bulbar impairment ("Speech" and "Swallowing" ALSFRS-r score ≤ 2) was present in 13 participants (30%) (online suppl. Fig. S1). Table 1 provides details on subjects' characteristics, respiratory function at the time of MI-E initiation, and current respiratory symptoms.

MI-E Characteristics

Details on MI-E initiation, training, and administration are shown in Table 2. Higher pressures were used during exsufflation compared to insufflation ($p < 0.001$), and exsufflation time was significantly longer than insufflation time ($p < 0.001$). Longer duration since treatment initiation was significantly related to higher insufflation ($p = 0.0003$) and exsufflation ($p = 0.001$) pressures. NIV use was associated with higher insufflation pressures ($p = 0.04$). Pressure settings according to neurological diagnosis are shown in online suppl. Figure S2. No statistically significant differences were noted in pressure, time, or flow settings or use of oscillations among the different diagnostic groups. However, severe bulbar impairment defined as a "Speech" and "Swallowing" ALSFRS-r score of ≤ 2 was associated with use of lower inspiratory pressures ($p = 0.004$). Detailed MI-E settings are shown in Table 3.

Patterns of MI-E Use – Reported Use

Fifteen participants (36%) reported using the MI-E rarely or never when not exacerbated (low users), 5 (12%) used the MI-E a few times per month up to once weekly, and 21 (50%) reported using the MI-E more than twice per week (regular users). The vast majority (94%) of all participants and 81% of low users reported using the device at least daily during an infectious episode, while 62% reported having used the device in emergency situations such as bronchoaspiration.

Subjects with MS reported the highest frequency of MI-E use (Fig. 1). Symptoms of cough, bronchial congestion, or bronchorrhea were associated with regular MI-E use ($p = 0.001$) and so was older age ($p = 0.011$). We found no association between reported regular use and participant gender, cognitive impairment, degree of bulbar impairment according to "Speech" and "Swallowing" ALS-

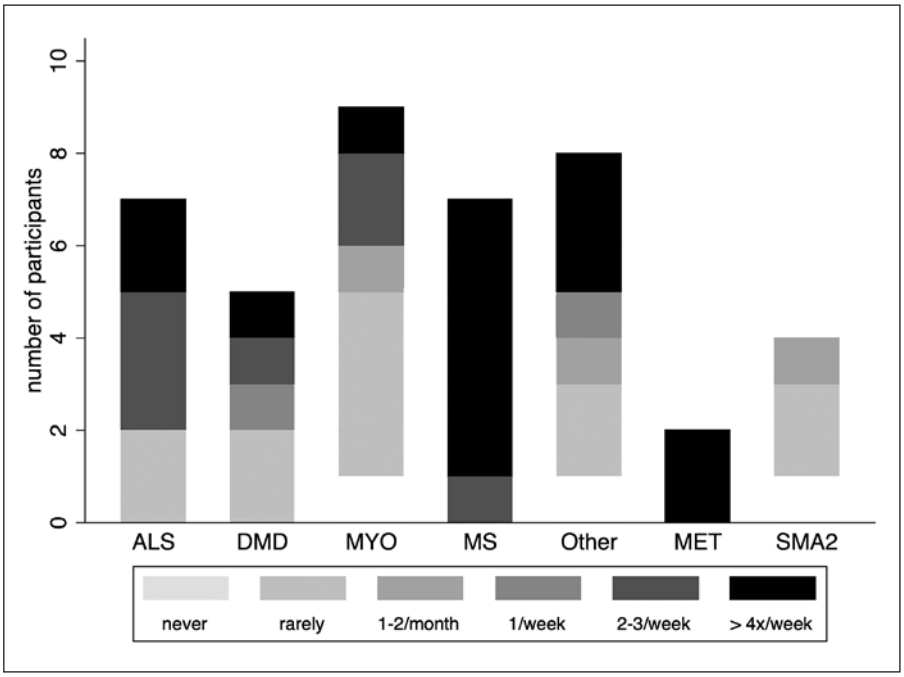

Fig. 1. Reported MI-E use and diagnostic groups. ALS, amyotrophic lateral sclerosis; DMD, Duchenne muscular dystrophy; MYO, muscular dystrophy (other than Duchenne); MS, multiple sclerosis; MET, metabolic myopathies; SMA2: spinal muscular atrophy type 2.

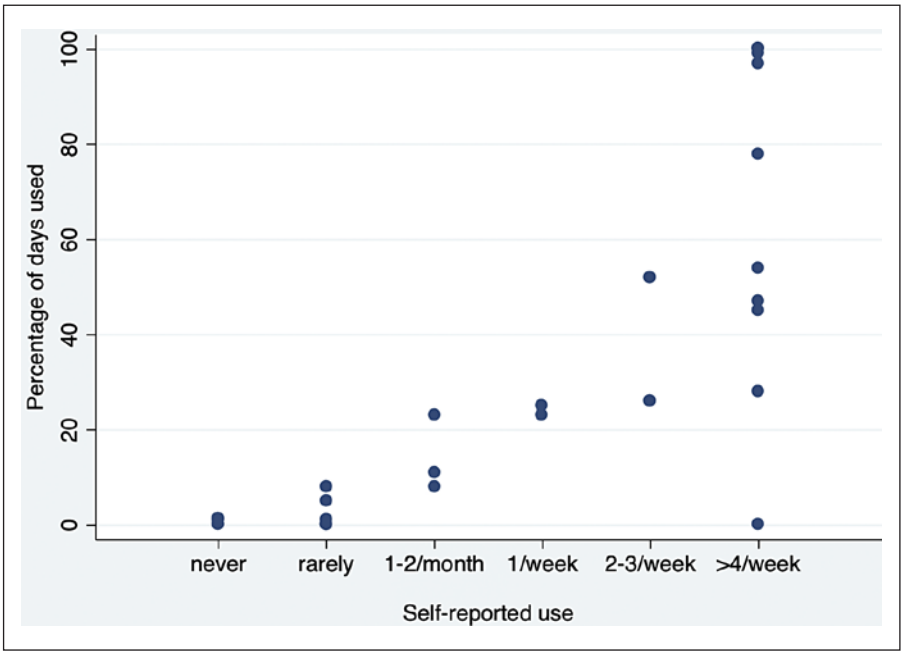

Fig. 2. Correlations between self-reported and objective use. Subjective use: subjects were asked to report the frequency of MI-E use when not exacerbated by choosing one of the following answers: never, rarely, 1-2/month, once a week, 2-3/week, >4/week. Objective use is expressed as the percentage of days used according to data downloads (r = 0.83). Data analysis could be performed only in 29 out of 42 cards due to technical issues.

FRS-r score, NIV use, baseline CPF. The pattern of use was not influenced by the living environment (home vs. institution), the number of persons trained, the type of administration (self-administration, administration by non-professional caregivers or by trained healthcare professionals), or the circumstances of initiation (elective vs. during exacerbation).

Explicit written information on usage recommendations could be found in medical notes for only 29 subjects. Among those, 15 (52%) had been instructed to use the device regularly (at least 2–3 times/week), while the remaining 14 (48%) were instructed to use the device as needed. Of those instructed to use the device regularly, only 5 (33.3%) reported using the device as prescribed

(online suppl. Fig. 3). Interestingly, 66.7% of those instructed to use the device as needed ended up reporting a regular use of the MI-E.

Patterns of MI-E Use – Objective Use

Information from 29 out of 42 SD cards could be analysed. The rest of the data were not accessible for technical reasons. We experienced difficulties downloading data from older CoughAssist™ E70 devices mostly due to wrong time settings of the device or to corrupted SD cards. Based on the obtained data downloads, median objective use was 23% of the days analysed. Fourteen participants (48%) used the device less than 15% of the days analysed (an equivalent of less than once weekly). Reported use correlated well with objective use based on MI-E data downloads ($r = 0.83$) but with a tendency towards an overestimation of reported use compared to objective data (Fig. 2).

As with reported use, subjects with MS employed the device most frequently (median 54% of days analysed) (online suppl. Fig. 4). The presence of cough, dyspnoea, and bronchorrhea was significantly associated with a more regular objective use of the device ($p < 0.0001$). No other associations were observed between objective use and the various parameters analysed, in particular baseline CPF and use of NIV.

Adverse Events

Twenty-one subjects (48%) reported at least one complication related to MI-E use. The most common reported adverse events were gastroesophageal reflux (23%), gastric distention (19%), palpitations (19%), chest pain (16%), blood-stained sputum (7%), and nausea (1%). One participant with congenital muscular dystrophy suffered an episode of pneumothorax requiring chest drainage. A direct link with the use of MI-E (insufflation pressure 30 cmH_2O, exsufflation pressure −30 cmH_2O) could not be established in this patient who was also on NIV which also increases the risk of barotrauma [42]. Nevertheless, cough assistance was interrupted in this case. We found no association between reported adverse events and reported or objective use of the device. Subjects with longer expiratory time were more likely to report an adverse event ($p = 0.02$). No other association between device settings and adverse events was noted.

Perceived Value of MI-E

The overall perception of MI-E was positive. The use of the device reportedly improved the respiratory health, breathing, and secretion clearance in 27 subjects (64%) and was considered most helpful in the event of bronchoaspiration and during chest infections. The majority of participants (78%) were satisfied with the treatment and would recommend it to someone with respiratory muscular weakness. Other positive comments included the feeling of reassurance and the impression that the treatment prevented or reduced hospitalizations. Frequent reported and objective use correlated with subjective respiratory improvement ($p = 0.03$) and with the overall perceived value of the treatment ($p = 0.04$), with no difference detected among the diagnostic groups. Lower exsufflation pressures were associated with higher overall satisfaction with the device ($p = 0.01$). Negative comments regarded mostly comfort and ease of use. Participants' answers and comments are summarized in online suppl. Table 2.

Discussion

In this cross-sectional study, we report a real-life experience of home MI-E use in adults with neurological conditions in Western Switzerland. The median objective MI-E use was 23% of days analysed, corresponding to using the device approximately 2 days per week. In a data-based analysis of adherence in a cohort of 181 NM patients, Chatwin and Simonds [39] report a median MI-E use of 60% of the days downloaded. The highest frequency of use in this study [39] was recorded in participants with spinal muscular atrophy type 1 and subjects with a tracheostomy, both of whom were not included in our population, making a direct quantitative comparison with our results difficult. In our study, participants with MS had a higher reported and objective adherence, although no significant differences were noted with regards to reported respiratory symptoms or bulbar dysfunction in this subgroup. The higher adherence could be related to the fact that the majority of MS subjects were institutionalized in a specialized long-term care facility for people with neurological disorders. At the whole population level, living in a long-term care facility was not associated with a more regular use of the device, but stratification according to institution specialization was not performed.

Consistent with the results of previous reports [38, 39], we observed that the frequency of MI-E use was strongly related to the presence of bronchial symptoms, while no association was observed between MI-E use and baseline CPF, underlying neurological diagnosis, or NIV use. Although a significant proportion of participants reported AEs related to MI-E use, the overall perception of the

treatment was positive and correlated with a regular use of the device. The strong association between regular use and satisfaction with MI-E is not surprising: On the one hand, a subjective and immediate benefit is a strong motivator to keep using a specific therapy; and, on the other hand, regular use might increase efficacy and improve satisfaction.

A factor potentially influencing treatment adherence is the underlying reason for MI-E prescription. According to current guidelines and expert opinions [32, 33, 36, 39], utilization of MI-E can be recommended on (a) a *daily* basis in order to avoid bronchial congestion, maintain chest wall compliance, and establish familiarity with the device and (b) in emergency situations for airway clearance. In Switzerland, according to national recommendations [36], the indication for MI-E is based on the inability to clear airway secretions in an effective manner as well as measurement of CPF. CPF values lower than 270 L/min should prompt the use of assisted cough techniques and the use of MI-E if the former fail. All patients are instructed to use the MI-E in case of an acute episode, such as bronchoaspiration or during a chest infection. Protocols based on oxygen saturation levels for emergency use of MI-E have been described [24, 43]. However, given that oximeters are not available to all patients in our population, in line with insurance coverage in Switzerland, participants were prompted to use the device in an emergency irrespective of oxygen saturation values, similar to other published real-life practices [39, 44]. Patients with chronically increased secretions are encouraged to employ the MI-E regularly as a preventive measure to avoid respiratory complications. Contrary to other published practices [35], in our study, not all subjects had received explicit instructions to use the device daily but were rather instructed to use the device as needed (for acute episodes) and regularly, if they had significant bronchorrhea or a very high risk of recurrent bronchoaspirations. However, written recommendations for regular MI-E use did not result in better adherence. The small number of participants and the limited information available from medical notes do not allow to ascertain whether more systematic recommendations could increase the frequency of MI-E use. In our study, a significant proportion of participants reported having used the device in emergency situations, notably after episodes of acute bronchoaspiration. In our opinion, this observation raises the question of the suitability of on-demand provision of MI-E as described in other countries [24], given the hyperacute nature of choking and bronchoaspiration episodes. However, daily versus continuous rental costs and the accessibility to MI-E should be taken into account when prescribing the device. As a preventive measure, the optimal frequency of MI-E use remains unknown [45]. Furthermore, on an individual level, the need for airway clearance may change with disease progression and added morbidities [35].

This study shows the importance of patients' perception for home MI-E use and underlines the need to individualize prescription in order to choose the most appropriate regime and to promote general adherence without overburdening patients and caregivers. As confidence in using the device and continuity among caregivers have been shown to influence successful implementation and use of MI-E [46], treatment initiation should be accompanied by appropriate and continuous training of all the persons involved in the use of the device [31].

With regards to device settings, higher exsufflation compared to insufflation pressures were used, as in previously published data [39, 47]. Device settings were manually titrated based on patient tolerance and secretion clearance and were subsequently switched, in most cases, to the automatic mode to facilitate home use. The preference for lower insufflation pressures is attributed to a better tolerance with avoidance of abdominal distension. At the same time, asymmetrically higher exsufflation (as compared to insufflation) pressures contribute towards an expiratory flow bias which results in more effective secretion clearance [31].

The pressures used in our group are lower than historically reported data [13, 48] and bench studies with artificial airways [49] but are similar to those reported in recent cohorts [17, 39, 47, 50, 51] and national surveys [44]. Relatively lower exsufflation pressures and shorter expiratory times were probably better tolerated and were associated with better satisfaction and fewer reported adverse events, underlying the need to titrate the settings to the lowest effective level. However, higher insufflation and exsufflation pressures might be needed in patients with invasive airway, as smaller tubes have higher resistance and thus require higher pressures to generate effective expiratory flows. We observed that longer usage of MI-E was associated with higher pressures, possibly reflecting the gradual up-titration of pressures secondary to disease progression, as well as an improved tolerance to higher pressures with familiarity with the device. As expected, higher insufflation pressures were used in subjects already on NIV, as they are more likely to have more pronounced inspiratory muscle weakness which per se reduced cough efficacy, irrespective of expiratory muscle or glottic function. An association between the use of NIV

and reported or objective adherence or overall satisfaction with the device was not demonstrated in this study, perhaps due to the small sample size.

We noted a tendency to use higher insufflation and exsufflation pressures in subjects with Duchenne muscular dystrophy; however, it was not statistically significant. No other differences concerning device settings were noted among the diagnostic groups, but severe bulbar dysfunction was associated with lower inspiratory pressures. In patients with ALS and bulbar symptoms, Andersen et al. [51] observed that the use of MI-E was associated with an adduction of supraglottic laryngeal structures during insufflation, possibly secondary to a hyper-responsive or dysregulated adductor reflex circuit [51]. In our real-life study, all settings were individually titrated in order to maximize secretion clearance and patient tolerance [52]. Consequently, it is likely that patients with bulbar dysfunction did not tolerate higher insufflation pressures due to the spasticity of upper airway. Interestingly, we did not observe a need for lower inspiratory flows in this subgroup of participants. Subjects with ALS did not require longer inspiratory times or lower inspiratory pressures and flows as suggested by Volpe et al. [53]. The scope of our work did not include assessment of synchronization with the device (via graphics analysis from the CoughAssist™ device and of MI-E-assisted exsufflation flows) [54]. However, numerous studies suggest that the sensitivity of these measurements is low in detecting upper airway collapse, and thus it does not predict MI-E efficacy [51, 55]. No difference in satisfaction with the MI-E devices, report of adverse events, or incidence of respiratory complications was noted in the ALS group compared to the other diagnostic groups.

Our study has several limitations. The limited size of this heterogeneous group of patients does not allow a generalization of study results. A selection bias cannot be excluded; patients who previously returned their MI-E device due to either intolerance, complications or lack of subjective benefit were not included in the study. We only studied one MI-E device model (CoughAssist E70™), as it was the only device available in Western Switzerland during the study period. It therefore remains an open question whether the results presented here, with regards to the perceived value of the treatment and its adverse events, can be generalized to other devices. Although the pharmacologic strategies for secretion management were not systematically retrieved from patient records, all patients were evaluated by the specialized phoniatrics team and were followed, if indicated, by a speech therapist, as per current guidelines [32–38].

In our study, we used unstructured questionnaires for the assessment of bronchial symptoms. However, available questionnaires (such as the Leicester cough questionnaire [56] or the cough and sputum assessment questionnaire [57]) are not validated for patients with NM or neurological diseases and measure bronchial symptoms with a short-term recall (2 and 1 weeks, respectively). Another limitation of the study is the limited number of data downloads that could be obtained from the MI-E devices. Nevertheless, reported use correlated well with objective use based on data downloads. The observed tendency of overestimation of self-reported use underlines the importance of determining adherence objectively in a research context. Further studies are needed to demonstrate the added benefit of a systematic analysis of graphics and data from MI-E devices in everyday clinical practice in terms of following adherence and adjusting device settings.

Conclusion

The results of our experience with home MI-E demonstrate that a higher use of home MI-E is associated with higher symptom burden and overall satisfaction with the device. Patients without substantial bronchorrhea might not use the MI-E regularly but might still need to use the device at home during acute events. Therefore, familiarity with the MI-E via appropriate and repeated practical training is essential. Prospective studies including high-quality data acquisition and validated patient-reported outcomes are highly desirable in order to understand which factors influence treatment adherence.

Acknowledgments

The authors would like to thank the Swiss Lung Association and M. P. Pasquina (Division of Pulmonary Diseases, Dept of Medicine, Geneva University Hospitals) for their contribution in contacting participants and providing access to MI-E data. We also thank Drs L. Burdet, B. Egger, M-M. Friberg, A. Pasche, and J-F. Vodoz for providing valuable clinical information and Mr. Ballabeni (Centre for Clinical Research, Lausanne University Hospital) for his help with statistical analysis. We are grateful to all subjects and their families for their kind cooperation in this study.

Statement of Ethics

Written informed consent was obtained from all participants and from the parents/guardians/next of kin for all vulnerable patients. The study protocol was approved by the Ethics Committee of the Canton of Vaud (CER-VD 2019-01114). The study was con-

ducted in accordance with the principles of the Declaration of Helsinki. Clinical Trial Registration: NCT04729920 (Clinicaltrials.org).

Conflict of Interest Statement

GM, JPJ, CVG, and MP declare no conflicts of interest. RH has received honoraria from ResMed, Philips, and Inspire and participates on the advisory board/data safety monitoring board of Nyxoah, Philips, Dreem.

Author Contributions

GM was responsible for literature search and data collection and analysis. GM, RH, and MP were responsible for the study design and prepared the manuscript. JPJ contributed to data collection and manuscript preparation. CvG reviewed the manuscript. All authors reviewed and approved the final version of the manuscript.

Funding Sources

This study was supported by a fund from the Lung Association of the Canton of Vaud, Switzerland, awarded to GM, MP, and RH.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author (Georgia Mitropoulou, Georgia.mitropoulou@chuv.ch) upon reasonable request. Further enquiries can be directed to the corresponding author.

References

1 Bach JR. Mechanical insufflation-exsufflation. Comparison of peak expiratory flows with manually assisted and unassisted coughing techniques. Chest. 1993;104(5):1553–62.
2 Mustfa N, Aiello M, Lyall RA, Nikoletou D, Olivieri D, Leigh PN, et al. Cough augmentation in amyotrophic lateral sclerosis. Neurology. 2003;61(9):1285–7.
3 Chatwin M, Ross E, Hart N, Nickol AH, Polkey MI, Simonds AK. Cough augmentation with mechanical insufflation/exsufflation in patients with neuromuscular weakness. Eur Respir J. 2003;21(3):502–8.
4 Fauroux B, Guillemot N, Aubertin G, Nathan N, Labit A, Clement A, et al. Physiologic benefits of mechanical insufflation-exsufflation in children with neuromuscular diseases. Chest. 2008;133(1):161–8.
5 Kim SM, Choi WA, Won YH, Kang SW. A comparison of cough assistance techniques in patients with respiratory muscle weakness. Yonsei Med J. 2016;57(6):1488–93.
6 Morrow B, Zampoli M, van Aswegen H, Argent A. Mechanical insufflation-exsufflation for people with neuromuscular disorders. Cochrane Database Syst Rev. 2013(12):CD010044.
7 Winck JC, Goncalves MR, Lourenco C, Viana P, Almeida J, Bach JR. Effects of mechanical insufflation-exsufflation on respiratory parameters for patients with chronic airway secretion encumbrance. Chest. 2004;126(3):774–80.
8 Bach JR, Gimenez GC, Chiou M. Mechanical in-exsufflation-expiratory flows as indication for tracheostomy tube decannulation: case studies. Am J Phys Med Rehabil. 2019;98(3):e18–e20.
9 Bach JR, Barrow SE, Goncalves M. A historical perspective on expiratory muscle aids and their impact on home care. Am J Phys Med Rehabil. 2013;92(10):930–41.
10 Leith D In: Brain JD, Proctor D, Reid L, editors. Lung biology in health and disease: respiratory defense mechanisms, part 2. Cough New York: Marcel Dekker; 1977. p. 545–92.
11 Barach AL, Beck GJ, Bickerman HA, Seanor HE, Smith W. Physical methods simulating mechanisms of the human cough. J Appl Physiol. 1952;5(2):85–91.
12 Homnick DN. Mechanical insufflation-exsufflation for airway mucus clearance. Respir Care. 2007;52(10):1296–305; discussion 1306–7.
13 Barach AL, Beck GJ, Bickerman HA, Seanor HE. Physical methods simulating cough mechanisms use in poliomyelitis, bronchial asthma, pulmonary emphysema, and bronchiectasis. J Am Med Assoc. 1952;150(14):1380–90.
14 Bach JR, Ishikawa Y, Kim H. Prevention of pulmonary morbidity for patients with Duchenne muscular dystrophy. Chest. 1997;112(4):1024–8.
15 Bach JR, Baird JS, Plosky D, Navado J, Weaver B. Spinal muscular atrophy type 1: management and outcomes. Pediatr Pulmonol. 2002;34(1):16–22.
16 Bach JR. Amyotrophic lateral sclerosis: prolongation of life by noninvasive respiratory AIDS. Chest. 2002;122(1):92–8.
17 Vianello A, Corrado A, Arcaro G, Gallan F, Ori C, Minuzzo M, et al. Mechanical insufflation-exsufflation improves outcomes for neuromuscular disease patients with respiratory tract infections. Am J Phys Med Rehabil. 2005;84(2):83–8; discussion 89–91
18 Miura T, Takami A, Makino M, Ishikawa A, Ishikawa Y. Rate of oral intake and effects of mechanical insufflation-exsufflation on pulmonary complications in patients with duchenne muscular dystrophy. J Phys Ther Sci. 2017;29(3):487–90.
19 Crew JD, Svircev JN, Burns SP. Mechanical insufflation-exsufflation device prescription for outpatients with tetraplegia. J Spinal Cord Med. 2010;33(2):128–34.
20 Rafiq MK, Shaw PJ. Cough assistance to clear lungs of ALS patients with severe bulbar dysfunction: not a good idea. Amyotroph Lateral Scler Frontotemporal Degener. 2015;16(7–8):534–5.
21 Tzeng AC, Bach JR. Prevention of pulmonary morbidity for patients with neuromuscular disease. Chest. 2000;118(5):1390–6.
22 Mahede T, Davis G, Rutkay A, Baxendale S, Sun W, Dawkins HJS, et al. Use of mechanical airway clearance devices in the home by people with neuromuscular disorders: effects on health service use and lifestyle benefits. Orphanet J Rare Dis. 2015;10:54.
23 Veldhoen ES, Verweij-van den Oudenrijn LP, Ros LA, Hulzebos EH, Papazova DA, van der Ent CK, et al. Effect of mechanical insufflation-exsufflation in children with neuromuscular weakness. Pediatr Pulmonol. 2020;55(2):510–3.
24 Vitacca M, Paneroni M, Trainini D, Bianchi L, Assoni G, Saleri M, et al. At home and on demand mechanical cough assistance program for patients with amyotrophic lateral sclerosis. Am J Phys Med Rehabil. 2010;89(5):401–6.
25 Bach JR, Sinquee DM, Saporito LR, Botticello AL. Efficacy of mechanical insufflation-exsufflation in extubating unweanable subjects with restrictive pulmonary disorders. Respir Care. 2015;60(4):477–83.
26 Bach JR, Goncalves MR, Hamdani I, Winck JC. Extubation of patients with neuromuscular weakness: a new management paradigm. Chest. 2010;137(5):1033–9.

27 Sancho J, Servera E, Vergara P, Marin J. Mechanical insufflation-exsufflation vs. tracheal suctioning via tracheostomy tubes for patients with amyotrophic lateral sclerosis: a pilot study. Am J Phys Med Rehabil. 2003;82(10):750–3.
28 Moran FC, Spittle AJ, Delany C. Lifestyle implications of home mechanical insufflation-exsufflation for children with neuromuscular disease and their families. Respir Care. 2015;60(7):967–74.
29 Travlos V, Drew K, Patman S. The value of the CoughAssist® in the daily lives of children with neuromuscular disorders: experiences of families, children and physiotherapists. Dev Neurorehabil. 2016;19(5):321–6.
30 Dale CM, McKim D, Amin R, Carbone S, Fisher T, Goldstein R, et al. Education experiences of adult subjects and caregivers for mechanical insufflation-exsufflation at home. Respir Care. 2020;65(12):1889–96.
31 Chatwin M, Toussaint M, Goncalves MR, Sheers N, Mellies U, Gonzales-Bermejo J, et al. Airway clearance techniques in neuromuscular disorders: a state of the art review. Respir Med. 2018;136:98–110.
32 Birnkrant DJ, Bushby K, Bann CM, Alman BA, Apkon SD, Blackwell A, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. Lancet Neurol. 2018;17(4):347–61.
33 Finkel RS, Mercuri E, Meyer OH, Simonds AK, Schroth MK, Graham RJ, et al. Diagnosis and management of spinal muscular atrophy: Part 2: pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics. Neuromuscul Disord. 2018;28(3):197–207.
34 Strickland SL, Rubin BK, Drescher GS, Haas CF, O'Malley CA, Volsko TA, et al. AARC clinical practice guideline: effectiveness of nonpharmacologic airway clearance therapies in hospitalized patients. Respir Care. 2013;58(12):2187–93.
35 Motor neurone disease: assessment and management National institute for health and care excellence. London: NationalClinical Guidelines; 2016.
36 Janssens JP, Michel F, Schwarz EI, Prella M, Bloch K, Adler D, et al. Long-term mechanical ventilation: recommendations of the Swiss society of pulmonology. Respiration. 2020:1–36.
37 Georges M, Perez T, Rabec C, Jacquin L, Finet-Monnier A, Ramos C, et al. Proposals from a French expert panel for respiratory care in ALS patients. Respir Med Res. 2022;81:100901.
38 EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis; Andersen PM, Abrahams S, Borasio GD, de Carvalho M, Chio A, et al. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS)--revised report of an EFNS task force. Eur J Neurol. 2012;19(3):360–75.
39 Chatwin M, Simonds AK. Long-term mechanical insufflation-exsufflation cough assistance in neuromuscular disease: patterns of use and lessons for application. Respir Care. 2020;65(2):135–43.
40 Cedarbaum JM, Stambler N, Malta E, Fuller C, Hilt D, Thurmond B, et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. BDNF ALS Study Group (Phase III). J Neurol Sci. 1999;169(1–2):13–21.
41 Volanti P, Cibella F, Sarva M, De Cicco D, Spanevello A, Mora G, et al. Predictors of non-invasive ventilation tolerance in amyotrophic lateral sclerosis. J Neurol Sci. 2011;303(1–2):114–8.
42 Suri P, Burns SP, Bach JR. Pneumothorax associated with mechanical insufflation-exsufflation and related factors. Am J Phys Med Rehabil. 2008;87(11):951–5.
43 Bach JR, Alba AS. Intermittent abdominal pressure ventilator in a regimen of noninvasive ventilatory support. Chest. 1991;99(3):630–6.
44 Rose L, Adhikari NK, Poon J, Leasa D, McKim DA, CANuVENT Group; Cough augmentation techniques in the critically ill: a Canadian national survey. Respir Care. 2016;61(10):1360–8.
45 Morrow B, Argent A, Zampoli M, Human A, Corten L, Toussaint M. Cough augmentation techniques for people with chronic neuromuscular disorders. Cochrane Database Syst Rev. 2021;4:CD013170.
46 Siewers V, Holmoy T, Frich JC. Experiences with using mechanical in–exsufflation in amyotrophic lateral sclerosis. Eur J Physiother. 2013;15(4):201–7.
47 Hov B, Andersen T, Hovland V, Toussaint M. The clinical use of mechanical insufflation-exsufflation in children with neuromuscular disorders in Europe. Paediatr Respir Rev. 2018;27:69–73.
48 Bach JR, Alba AS, Saporito LR. Intermittent positive pressure ventilation via the mouth as an alternative to tracheostomy for 257 ventilator users. Chest. 1993;103(1):174–82.
49 Guerin C, Bourdin G, Leray V, Delannoy B, Bayle F, Germain M, et al. Performance of the coughassist insufflation-exsufflation device in the presence of an endotracheal tube or tracheostomy tube: a bench study. Respir Care. 2011;56(8):1108–14.
50 Lacombe M, Del Amo Castrillo L, Bore A, Chapeau D, Horvat E, Vaugier I, et al. Comparison of three cough-augmentation techniques in neuromuscular patients: mechanical insufflation combined with manually assisted cough, insufflation-exsufflation alone and insufflation-exsufflation combined with manually assisted cough. Respiration. 2014;88(3):215–22.
51 Andersen T, Sandnes A, Brekka AK, Hilland M, Clemm H, Fondenes O, et al. Laryngeal response patterns influence the efficacy of mechanical assisted cough in amyotrophic lateral sclerosis. Thorax. 2017;72(3):221–9.
52 Andersen T, Sandnes A, Hilland M, Halvorsen T, Fondenes O, Heimdal JH, et al. Laryngeal response patterns to mechanical insufflation-exsufflation in healthy subjects. Am J Phys Med Rehabil. 2013;92(10):920–9.
53 Volpe MS, Naves JM, Ribeiro GG, Ruas G, Amato MBP. Airway clearance with an optimized mechanical insufflation-exsufflation maneuver. Respir Care. 2018;63(10):1214–22.
54 Sancho J, Ferrer S, Bures E, Fernandez-Presa L, Banuls P, Gonzalez MC, Signes-Costa J. Waveforms analysis in patients with amyotrophic lateral sclerosis for enhanced efficacy of mechanically assisted coughing. Respir Care. 2022;67(10):1226–35.
55 Lacombe M, Bore A, Amo Castrillo LD, Boussaid G, Falaize L, Vlachos E, et al. Peak cough flow fails to detect upper airway collapse during negative pressure titration for cough-assist. Arch Phys Med Rehabil. 2019;100(12):2346–53.
56 Birring SS, Prudon B, Carr AJ, Singh SJ, Morgan MDL, Pavord ID. Development of a symptom specific health status measure for patients with chronic cough: Leicester Cough Questionnaire (LCQ). Thorax. 2003;58(4):339–43.
57 Crawford B, Monz B, Hohlfeld J, Roche N, Rubin B, Magnussen H, et al. Development and validation of a cough and sputum assessment questionnaire. Respir Med. 2008;102(11):1545–55.