The Addition of Mechanical Insufflation/Exsufflation Shortens Airway-Clearance Sessions in Neuromuscular Patients With Chest Infection

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BACKGROUND: Mechanical insufflation/exsufflation (in-exsufflation) increases peak cough flow and may improve sputum clearance. No studies have compared current respiratory physiotherapy practice (manual percussion, shaking, and assisted cough) plus mechanical in-exsufflation to current physiotherapy practice without in-exsufflation in noninvasive-ventilation (NIV) dependent neuromuscular patients with an acute respiratory-tract infection. We hypothesized that airway clearance in these patients would be more effective with in-exsufflation, compared to without in-exsufflation. METHODS: Eight patients (6 male), median age 21.5 y (range 4–44 y). All had sputum retention, with an elevated C-reactive protein of 113 mg/L (range 13–231 mg/L) and a white-cell count of 14×10^9 cells/L (range $7–25\times10^9$ cells/L). Patients underwent a 2-day randomized crossover treatment program, with in-exsufflation for one session and without in-exsufflation for the second, with a reverse-crossover on the next day. Treatment time after 30 min (or earlier if sputum clearance was complete) was recorded. Outcome measures were heart rate, pulse oximetry (S_{pO_2}), transcutaneous carbon dioxide tension (P_{tcCO_2}), and independently assessed auscultation score. Patients rated effectiveness on a visual analog scale. RESULTS: Treatment time after 30 min was significantly shorter with in-exsufflation, versus without in-exsufflation session ($30 + 0 = 30$ min (range 0–26 min) vs $30 + 17 = 47$ min (range 0–35 min) ($P = .03$). There was a significant improvement in auscultation score in both groups (with in-exsufflation 2.9 ± 1.9 to 1.8 ± 2.0, $P = .02$; without in-exsufflation 3.4 ± 2.0 to 2.3 ± 2.2, $P = .007$). Visual-analog-scale score for the amount of sputum cleared in both treatment groups showed a decline ($P < .05$). There was no difference in mean heart rate, S_{pO_2}, or P_{tcCO_2} with either treatment. CONCLUSIONS: This is a short-term study of the use of in-exsufflation as a supplement to standard NIV plus physiotherapy in a small group of patients with neuromuscular disease. The addition of mechanical in-exsufflation shortened airway-clearance sessions. The device appeared to be safe and well tolerated, and may provide additional benefit to patients with neuromuscular disease and upper-respiratory-tract infection; further studies are indicated. *Key words: spinal muscular atrophy, Duchenne muscular dystrophy, chest physiotherapy, cough assist, nocturnal hypoventilation.* [Respir Care 2009;54(11):1473–1479. © 2009 Daedalus Enterprises]

Introduction

Effective cough is a protective mechanism against respiratory-tract infections. In patients with respiratory muscle weakness due to neuromuscular disease, respiratory-tract infections are the commonest cause of hospital admission.[1] Neuromuscular-disease patients may have impaired cough and a reduction in peak cough flow[2] as a

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result of inspiratory muscle weakness and expiratory muscle weakness, which causes a reduction in the pressure available to drive the cough maneuver.[3]

There are 3 main components to a cough: deep inspiration, glottic closure, and effective contraction of the expiratory muscles.[4] An impairment of any one can cause reduced cough efficacy. Bulbar dysfunction produces an inability to close and rapidly open the glottis during a cough, even in the presence of normal respiratory muscle function. In patients with amyotrophic lateral sclerosis[5] and Duchenne muscular dystrophy[6,7] the extent of inspiratory and expiratory muscle dysfunction is similar, and in some conditions, such as spinal muscular atrophy, expiratory muscle weakness can be the predominant feature.[7,8] Decreased expiratory muscle strength affects expiratory air flow, and this leads to a decrease in cough efficacy and secretion clearance.[6]

Recommended physiotherapy treatment for patients with neuromuscular disease who require noninvasive ventilation (NIV) at Royal Brompton Hospital is a modified active-cycle-of-breathing technique.[9] This can be described as cycles of deep breathing, where a noninvasive ventilator has the pressure increased to augment a greater tidal volume. Either percussion or shaking (to loosen secretions) is then performed, followed by a period of breathing on the ventilator set at the patient's normal pressure. An assisted cough is then initiated manually, augmented by a physiotherapist performing inward and upward pressure on the lower thorax, after the patient has had a deep inspiration delivered by the noninvasive ventilator.[9] An alternative method of treatment is the addition of a mechanical insufflator/exsufflator (CoughAssist, Philips Respironics, Murrysville, Pennsylvania). This device clears secretions by (gradually) applying a positive pressure to the airway (insufflation), then rapidly shifting to negative pressure. The rapid shift in pressure produces a high expiratory flow, simulating a natural cough.

NIV has been shown to improve physiotherapy tolerance and assist in the prevention of oxygen desaturation in a pediatric cystic fibrosis population.[10] The efficacy of physiotherapy on NIV has not been formally evaluated in neuromuscular-disease patients, despite the fact many become dependent on NIV during an acute respiratory-tract infection. Mechanical insufflation/exsufflation (in-exsufflation) has been evaluated in neuromuscular-disease patients in a physiological study, which showed that all methods of cough augmentation were acceptable to patients, but mechanical in-exsufflation increased peak cough flow rate the greatest.[2] The use of mechanical in-exsufflation has not been evaluated either prospectively or in a randomized study. It is important from a health-service economic perspective to evaluate the addition of mechanical in-exsufflation over and beyond the provision of physiotherapy and NIV.

We hypothesized that individuals with neuromuscular disease who present with a respiratory-tract infection will have a more effective airway-clearance session with the addition of mechanical in-exsufflation, compared to current respiratory physiotherapy practice on NIV. Thus, the aim of the study is to compare current respiratory physiotherapy practice without in-exsufflation to current respiratory physiotherapy practice with the addition of in-exsufflation on physiological variables, including oxygen saturation measured via pulse oximetry (S_{pO_2}), transcutaneous carbon dioxide (P_{tcCO_2}), and patient satisfaction evaluated via visual analog scale, in individuals with neuromuscular disease who had an acute respiratory-tract infection.

Methods

Subjects

The study was approved by the local ethics committee, and all subjects and/or parents gave informed consent. Subjects >3 years of age were recruited from patients admitted to the adult and pediatric wards at the Royal Brompton Hospital with an acute respiratory-tract infection, which was defined by at least three of the following: decreased oxygen saturation < 94%; sputum production (patient producing yellow or green secretions when normally has none); increased shortness of breath (subjectively reported or increase in resting respiratory rate of > 5 breaths/min); pyrexia (temperature > 38°C); signs of infection on chest radiograph (collapse or consolidation) or auscultation (presence of crackles in lung fields); elevated C-reactive protein (> 5 mg/L) or white-cell count ($> 10\times10^9$ cells/L). Exclusion criteria included the presence of a pneumothorax, tracheostomy, severe bulbar weakness, severe uncontrolled asthma, rapidly progressive chest infection with failure to control arterial blood gas tension using NIV, and patients referred for weaning of NIV after intubation. All patients had confirmed diagnoses of a neuromuscular disease and were users of nocturnal NIV.

Study Protocol

Patients were randomized to group 1 or group 2. Patients randomized to group 1 received on day 1 a morning treatment without in-exsufflation and an afternoon treatment with in-exsufflation, and on day 2 a morning treatment with in-exsufflation and an afternoon treatment without in-exsufflation. Group 2 received the same treatments in the reverse order. Airway-clearance sessions were standardized to prevent treatment bias. Individuals had their randomized treatment at standardized times, as in other airway-clearance studies.[11] If a patient required evening treatments, this was provided as conventional physiother-

apy. If a patient required treatment earlier than the planned treatment time, this was provided, and further treatment times were adjusted accordingly. In our experience, airway-clearance treatment lasts at least 30 min, and because of this, patients were assessed at 30 min (or earlier if there were no secretions present). Patients then continued to have treatment until they were fatigued or there were no longer any secretions produced. It is important to have a standardized reassessment to prevent subjectivity and patient fatigue causing bias.

The without in-exsufflation treatment consisted of modified active-cycle-of-breathing technique on NIV.[9] Typically the active-cycle-of-breathing techniques consist of breathing control (relaxed normal breathing from the diaphragm), followed by 4 or 5 thoracic-expansion exercises to mobilize secretions via collateral ventilation, with or without manual techniques (clapping and shaking), breathing control, and then the forced-expiration technique.[12] This cycle is repeated to mobilize secretions to the mouth, and aims to clear secretions without uncontrolled coughing. In patients with neuromuscular disease this technique can be modified by changing the settings on their noninvasive ventilator to provide an increased tidal volume for thoracic-expansion exercises and for the pre-insufflation part of the cough. The expiratory component of the cough was performed with a manual abdominal assisted cough. Patients were treated for 30 min and then reassessed. If treatment was incomplete at reassessment, the session was continued and the additional treatment time was recorded.

The with in-exsufflation treatment consisted of a treatment session as described above with the addition of in-exsufflation (in manual mode) during the cough maneuver, along with a manual abdominal assisted cough. The in-exsufflation settings were +20 cm H_2O (range +15 to +35 cm H_2O) and −20 cm H_2O (range −20 to −40 cm H_2O), insufflation time 2–4 s, and exsufflation time 4–5 s. As in the without in-exsufflation treatments, patients were treated for 30 min and then reassessed. If treatment was incomplete at reassessment, the session was continued and additional treatment time was recorded.

Physiological Measurements

Throughout each treatment session, heart rate, S_{pO_2}, and P_{tcCO_2} were recorded.

Transcutaneous Carbon Dioxide. P_{tcCO_2} was measured using a standard gas analyzer (TCM3, Radiometer, Copenhagen, Denmark). Prior to the study the membrane was changed and a calibration was performed to 52 cm H_2O, using standard CO_2 test gas mixtures. The P_{tcCO_2} electrode was then heated to 42.5°C and placed on the forearm, following careful skin preparation. The P_{tcCO_2} was allowed to reach equilibrium prior to commencement of the study. The Radiometer TINA system has been previously validated in our laboratory by comparison with simultaneous arterial blood gas sampling.[13]

Heart Rate and Oxygen Saturation. Heart rate and S_{pO_2} were measured via a probe attached to the patient's finger, using a Minolta Pulsox-3i pulse oximeter (Stowood Scientific Instruments, Beckley, Oxford, United Kingdom). The sampling frequency of this device was 1 Hz, and the signal was averaged over 2–5 s. The device displayed the data every second. The output of the oximeter was analyzed using commercial software (Download 2001, Stowood Scientific Instruments, Beckley, Oxford, United Kingdom).

Treatment Time

Time points used for analysis were treatment time up to the 30 min reassessment (some treatment sessions did not require a full 30 min [$n = 4$]) and continued treatment time.

Subjective Measurements

Auscultation. Air entry was evaluated before and after treatments via auscultation while on NIV. All auscultation was verified by a physiotherapist blinded to the intervention. The physiotherapist has worked as a respiratory physiotherapist for more than 10 years and has worked with ventilated adults and children for more than 9 years. Air entry was compared right to left in the upper, middle, and lower zones. If any added sounds were present, these were recorded and classified as wheeze or crackles: one point was given to decreased air entry in one of the 6 areas auscultated, and one point for crackles. A maximum of 12 points indicated very poor air entry, with a large volume of sputum present. A low score indicated good air entry, with no secretions.

Visual Analog Scale. The acceptability of each treatment was measured on a visual analog scale.[14] Patients were asked to rate each of the following questions. How comfortable are you? How breathless are you? How happy are you feeling? How much sputum is present? How tired are you feeling? Each of the 5 items was scored separately on a 10-point score (0 = optimal outcome, 10 = unfavorable outcome). The visual analog scale was evaluated 1–2 min before treatment and 1–2 min after treatment.

Statistical Analysis

Data were tested for normality using the Kolmogorov-Smirnov test. Where data were normally distributed, values were expressed as mean ± SD. Non-normally distributed data are expressed as median and interquartile range.

Table 1. Patient Characteristics

Patient Identification	Diagnosis	Sex	Age (y)	Duration of NIV use (mo)	NIV Use per 24 h	C-Reactive Protein (mg/L)	White-Cell Count ($\times 10^9$ cells/L)	Sputum Growth	Chest Radiograph Changes
A	Duchenne muscular dystrophy	M	27	44	> 20 h	334	15.1	None	N
B	Spinal muscular atrophy type II	F	44	1	Occasional	26	24.7	*Staphylococcus aureus*	Y
C	Spinal muscular atrophy type II	M	12	130	> 23 h	ND	ND	*Streptococcus pneumoniae* *Pseudomonas aeruginosa*	N
D	Duchenne muscular dystrophy	M	27	18	> 23 h	213	7.7	None	N
E	Duchenne muscular dystrophy	M	21	21	Nocturnal	144	10.3	*Pseudomonas aeruginosa*	Y
F	Spinal muscular atrophy type II	F	4	5	Nocturnal	ND	22.3	None	Y
G	Duchenne muscular dystrophy	M	22	12	Nocturnal	113	13.6	None	Y
H	Congenital myopathy	M	21	43	Nocturnal	60	6.7	None	Y

NIV = noninvasive ventilation
ND = no data collected

Differences between the 2 groups (with and without in-exsufflation) were analyzed using parametric tests or non-parametric tests. For comparison of 2 means, a Student's paired *t* test analysis (2-tailed) was used, or a Wilcoxon rank-sum test was used. The null hypothesis (ie, there was no difference in heart rate, S_{aO_2}, and P_{tcCO_2} during either intervention [with or without in-exsufflation]) was rejected at $P > .05$. The power of the study was calculated as 82% at $n = 8$, given a difference in the mean for the treatment time of 13 ± 11 min between the without in-exsufflation and the with in-exsufflation treatments, at an alpha = .05 significance level.

Results

Eight patients (6 male) with neuromuscular disease ($n = 4$ Duchenne muscular dystrophy, $n = 3$ spinal muscular atrophy type II, $n = 1$ congenital myopathy), median age 21.5 y (range 4–44 y) participated; patient demographics are in Table 1. All had difficulty clearing secretions and a symptomatic respiratory-tract infection that required nearly continuous NIV. Patients had an elevated C-reactive-protein level median of 113 mg/L (range 13–321 mg/L) and white-cell count of 14×10^9 cells/L (range 7–25×10^9 cells/L). Sputum culture was positive in 3.

Physiological Measurements

There were no differences in group mean S_{pO_2} or P_{tcCO_2} recorded, and no difference in heart rate during either treatment. Similar inspiratory pressures on the ventilator and the insufflation during in-exsufflation were used (21 ± 5.6 cm H_2O and 21 ± 5.6 cm H_2O, respectively). Two patients (C and F) required supplementary oxygen at 2 L/min; this flow rate remained the same for the 2 days of the study, indicating standardization with respect to inspiratory pressures delivered and oxygenation.

Treatment Parameters

All treatments lasted for a minimum of 30 min, except for 2 with in-exsufflation sessions and 2 without in-exsufflation sessions where the patients were free from secretions prior to the standard reassessment point. Subsequent treatment time after 30 min was significantly shorter in the with in-exsufflation group (0 min, range 0–26 min) than in the without in-exsufflation group (17 min, range 0–35 min) ($P = .03$) (Fig. 1).

There was a significant decrease in auscultation score for both groups (without in-exsufflation 3.4 ± 2.0 to 2.3 ± 2.2, $P = .007$; with in-exsufflation 2.9 ± 1.9 to 1.8 ± 2.0, $P = .02$), indicating better air entry and fewer secretions present with both forms of treatment.

Visual-Analog-Scale Scores

The visual-analog-scale scores for the changes in secretions, comfort, breathlessness, mood, and fatigue are shown in Figure 2. Patients recorded a statistically significant

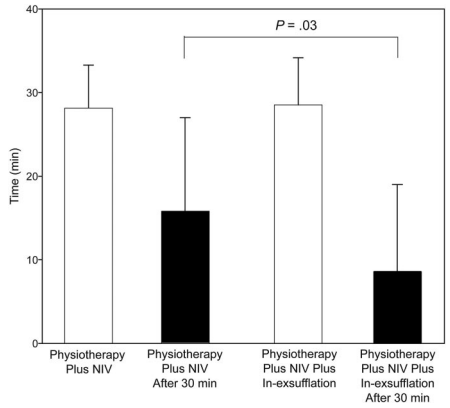

Fig. 1. Mean ± SD treatment time for physiotherapy plus noninvasive ventilation (NIV) without insufflation/exsufflation (in-exsufflation) and with in-exsufflation, prior to the first assessment (white bars). The black bars show the mean and SD treatment time after the initial assessment at 30 min.

decline in the amount of secretions they felt were present (without in-exsufflation: before 4.4 ± 2.5 and after 3.0 ± 1.4, $P = .03$; with in-exsufflation: before 4.0 ± 2.2 and after 1.7 ± 0.4, $P = .03$). Visual-analog-scale scores for fatigue following treatment in the with-in-exsufflation group were significantly higher (3.2 ± 2.2 before and 5.1 ± 2.6 after, $P = .005$), indicating a higher sensation of fatigue after the in-exsufflation treatment, which may be attributed to long exsufflation times.

Discussion

This is the first prospective study of mechanical in-exsufflation in acute chest infection. The results indicate that there is a role for mechanical in-exsufflation in assisting secretion clearance. With and without in-exsufflation, a similar amount of secretions were cleared, but treatment times were longer without in-exsufflation.

The key outcome measures in the present study were physiological variables (S_{pO_2}, P_{tcCO_2}, and heart rate). There were no differences between without in-exsufflation and with in-exsufflation in any of these variables, indicating that both methods of treatment are not detrimental to S_{pO_2}, P_{tcCO_2}, or heart rate, and that neither treatment caused ventilatory instability in this group of frail patients.

Limitations of This Study

Every suitable neuromuscular-disease patient admitted to Royal Brompton Hospital with an acute respiratory-tract infection in 2003 through 2005 participated in this study. The numbers were unexpectedly small; one explanation for this is that respiratory care has improved in neuromuscular disease. For example, consensus statements[15-18] have led to centers that are managing individuals with neuromuscular disease to advocate that patients have influenza and pneumococcal vaccinations, and to provide them with an emergency course of antibiotics. Also, parents and caregivers are being taught conventional physiotherapy. As a result of this management, individuals are being managed successfully at home and not requiring admission. Interestingly, these ideas have been verified by work from Denmark[19]; those authors commented that the development of 2 specialist centers improved total respiratory care in patients with Duchenne muscular dystrophy.

All the patients had clinical evidence of acute respiratory-tract infection, diagnosed on multiple factors. It has been recently shown in a systematic review that C-reactive protein alone is neither sufficiently sensitive to rule out, nor sufficiently specific to rule in, infiltrate on chest ra-

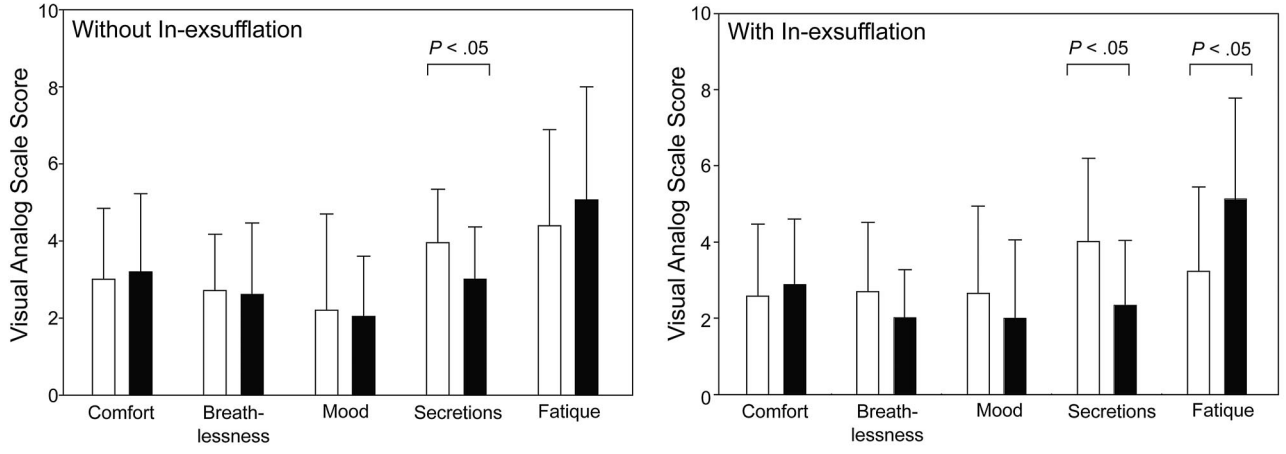

Fig. 2. Visual-analog-scale scores (mean and SD) before the intervention (white bars) and at first assessment (30 min or earlier if chest clear) (black bars). The lower the score the more favorable the outcome. There was a significant decline in the reported amount of secretions for both interventions. However, there was a significantly higher level of fatigue with the intervention (in-exsufflation).

diograph or bacterial etiology of lower-respiratory-tract infection.[20] Five out of 8 patients had definite radiologic changes on chest radiograph. Chest radiographs in these patients can be exceedingly difficult to interpret, as scoliosis can cause hyperinflated lung regions while other regions may be prone to chronic atelectasis, and this can obscure the true clinical picture. It is advisable that patients have a reference chest radiograph to aid diagnosis of acute radiologic changes.

Using sputum as a primary outcome is difficult in this group of patients, and any further studies will need to address this. Other studies of neuromuscular patients that have measured collected secretions have included patients with tracheostomies.[21,22] In the United Kingdom and at our center few neuromuscular patients have a tracheostomy (1% of our home-mechanical-ventilation patients),[23] and this number is smaller than that reported by other countries.[24]

Auscultation scores were verified by a physiotherapist who was not involved in the study. In our opinion, auscultation is the best marker of air entry and the presence of secretions. In this study the auscultation assessment was by a highly experienced respiratory physiotherapist, and we recognize that such experience may not be available in all centers.

Importance of Findings

No prospective or retrospective studies have evaluated NIV as an airway-clearance technique in neuromuscular-disease patients who use home NIV. Fauroux et al[10] investigated the effect of NIV as an airway-clearance technique in cystic-fibrosis patients and found far less fatigue in clearing secretions with the assistance of NIV. We felt it was important to treat these neuromuscular-disease patients on NIV in order to minimize fatigue. Unlike Fauroux et al,[10] the patients in the present study had a greater degree of respiratory muscle failure, and during an acute respiratory-tract infection they often became 24-hour ventilator-dependent.[1,25,26] An explanation for the increased ventilatory dependence during this period is the transient decrease in respiratory muscle strength, which can decrease oxygenation and increase P_{aCO_2}, as previously reported in a similar group of patients.[27] In the present study, patients often refused to come off the ventilator to carry out the respiratory muscle tests, so we were unable to objectively evaluate whether in-exsufflation affected fatigue. It is, however, important to note that we made no change to the ventilator settings; the patients were adequately supported with NIV to clear secretions effectively but prevent fatigue and decompensation.

We found a significant reduction in the treatment time at or after 30 min with in-exsufflation, compared to without in-exsufflation. Both sessions improved secretion clearance at 30 min, as judged via visual-analog-scale and auscultation scores. Interestingly, these patients rated fatigue higher with in-exsufflation.

The use of mechanical in-exsufflation in this study was in a CoughAssist-naïve group of patients with neuromuscular disease. This is a patient group that is likely to be admitted to local hospitals with a chest infection. We hope this study highlights some of the problems they may encounter. We feel it is important to start with lower pressures, as we did in this study, but the pressures should be rapidly increased to ensure an adequate cough.[28]

Conclusions

Both treatment methods appeared to be similarly efficacious and safe, with the limitations noted. In-exsufflation facilitated a shorter physiotherapy session in neuromuscular patients with acute respiratory-tract infection, although in-exsufflation was accompanied by a higher subjective feeling of fatigue. Studies of hospitalizations, hospital stay, and impact on lung function are warranted.

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