

# CHEST<sup>®</sup>

Official publication of the American College of Chest Physicians



## **Efficacy of Mechanical Insufflation-Exsufflation in Medically Stable Patients With Amyotrophic Lateral Sclerosis**

Jesús Sancho, Emilio Servera, Juan Díaz and Julio Marín

*Chest* 2004;125:1400-1405  
DOI 10.1378/chest.125.4.1400

The online version of this article, along with updated information and services can be found online on the World Wide Web at:  
<http://chestjournal.org/cgi/content/abstract/125/4/1400>

CHEST is the official journal of the American College of Chest Physicians. It has been published monthly since 1935. Copyright 2007 by the American College of Chest Physicians, 3300 Dundee Road, Northbrook IL 60062. All rights reserved. No part of this article or PDF may be reproduced or distributed without the prior written permission of the copyright holder (<http://www.chestjournal.org/misc/reprints.shtml>). ISSN: 0012-3692.

A M E R I C A N C O L L E G E O F  
 C H E S T  
P H Y S I C I A N S<sup>®</sup>

# Efficacy of Mechanical Insufflation-Exsufflation in Medically Stable Patients With Amyotrophic Lateral Sclerosis\*

Jesús Sancho, MD; Emilio Servera, MD, FCCP; Juan Díaz, RN; and Julio Marín, MD, FCCP

**Objective:** To determine under what circumstances the use of mechanical insufflation-exsufflation (MI-E) can generate clinically effective expiratory flows for airway clearance ( $> 2.7$  L/s) for clinically stable patients with amyotrophic lateral sclerosis (ALS).

**Materials and method:** Twenty-six consecutive patients with ALS were studied, 15 with severe bulbar dysfunction. Using a pneumotachograph and with the aid of an oronasal mask, we measured FVC, FEV<sub>1</sub>, peak cough flow (PCF), maximum insufflation capacity (MIC), PCF generated from a maximum insufflation MIC (PCF<sub>MIC</sub>), and PCF generated by MI-E (PCF<sub>MI-E</sub>). MI-E was delivered at  $\pm 40$  cm H<sub>2</sub>O. Maximum inspiratory pressure (P<sub>imax</sub>) and maximum expiratory pressure (P<sub>emax</sub>) at the mouth were also measured.

**Results:** Although both groups had a similar time from ALS symptom onset to diagnosis, statistical differences ( $p < 0.05$ ) were found between nonbulbar and bulbar patients in lung function and cough capacity parameters: FVC,  $2.58 \pm 1.24$  L vs  $1.62 \pm 0.74$  L; FEV<sub>1</sub>,  $2.26 \pm 1.18$  L vs  $1.54 \pm 0.69$  L; P<sub>imax</sub>,  $-93.45 \pm 47.47$  cm H<sub>2</sub>O vs  $-3.64 \pm 25.07$  cm H<sub>2</sub>O; P<sub>emax</sub>,  $140.45 \pm 75.98$  cm H<sub>2</sub>O vs  $69.93 \pm 32.14$  cm H<sub>2</sub>O; MIC,  $3.02 \pm 1.22$  L vs  $1.97 \pm 0.75$  L; PCF,  $5.91 \pm 2.55$  L/s vs  $3.42 \pm 1.44$  L/s; PCF<sub>MIC</sub>,  $6.68 \pm 2.71$  L/s vs  $4.00 \pm 1.48$  L/s; and PCF<sub>MI-E</sub>,  $4.34 \pm 0.82$  L/s vs  $3.35 \pm 0.77$  L/s. Four patients with bulbar dysfunction and MIC  $> 1$  L had PCF<sub>MI-E</sub>  $< 2.7$  L/s. The receiver operating characteristic (ROC) curve analysis showed PCF<sub>MIC</sub> of  $\leq 2.7$  L/s predicting those patients with PCF<sub>MI-E</sub>  $< 2.7$  L/s. The ROC curve analysis showed PCF<sub>MIC</sub>  $> 4$  L/s predicting those patients with PCF<sub>MIC</sub> greater than PCF<sub>MI-E</sub>.

**Conclusion:** MI-E is able to generate clinically effective PCF<sub>MI-E</sub> ( $> 2.7$  L/s) for stable patients with ALS, except for those with bulbar dysfunction who also have a MIC  $> 1$  L and PCF<sub>MIC</sub>  $< 2.7$  L/s who probably have severe dynamic collapse of the upper airways during the exsufflation cycle. Clinically stable patients with mild respiratory dysfunction and PCF<sub>MIC</sub>  $> 4$  L/s might not benefit from MI-E except during an acute respiratory illness. (CHEST 2004; 125:1400-1405)

**Key words:** amyotrophic lateral sclerosis; cough capacity; lung function test; mechanical insufflation-exsufflation; neuromuscular disease; noninvasive respiratory aids; noninvasive ventilation; peak cough flow

**Abbreviations:** ALS = amyotrophic lateral sclerosis; MIC = maximum insufflation capacity; MI-E = mechanical insufflation-exsufflation; NEP = negative pressure during tidal expiration; PCF = peak cough flow; PCF<sub>MI-E</sub> = peak cough flow generated by mechanical insufflation-exsufflation; PCF<sub>MIC</sub> = peak cough flow attained with maximum insufflation capacity; P<sub>emax</sub> = maximum expiratory pressure; P<sub>imax</sub> = maximum inspiratory pressure; ROC = receiver operating characteristic

Amyotrophic lateral sclerosis (ALS) is a progressive motorneuron disease. Inspiratory, expiratory, and upper airway muscles become impaired.<sup>1</sup>

\*From the Department of Respiratory Medicine, Hospital Clínico Universitario, Universitat de València, Valencia, Spain. The preliminary results of this study were presented at the IX Congress of the Sociedad Valenciana de Neumología, Oliva, Spain, April 2002, and received the award for the best poster presentation.

Manuscript received March 31, 2003; revision accepted September 1, 2003.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Emilio Servera MD, FCCP, Avda Blasco Ibáñez 84, E 46021 Valencia, Spain; e-mail: emilio.servera@uv.es

Respiratory complications, and especially airway secretion encumbrance from ineffective coughing, are the principal causes of morbidity and mortality.<sup>2</sup>

Coughing is a key defense mechanism of the airways. The effectiveness of mucus clearance is largely dependent on the magnitude of peak cough flows (PCFs).<sup>3</sup> Respiratory muscle weakness decreases PCF and, thereby, diminishes cough effectiveness. There are few data regarding a cutoff point for cough effectiveness. However, a PCF of  $< 2.7$  L/s has been proposed as indicating an ineffective cough on the basis of flows below this level resulting in extubation failure.<sup>4</sup> Baseline PCF values  $< 4.5$  L/s

have also been reported to be associated with a high risk for pulmonary complications during respiratory tract infections<sup>5</sup> because during chest infections the pressure generated by expiratory muscles is reduced<sup>6</sup> and, consequently, PCF decreases further. However these cutoff PCF values must be taken with caution and not as precise guidelines to predict cough failure, because they are not based on prospective trial results.

The use of inspiratory and expiratory aids has been reported to reduce the risk of pulmonary complications and prolong survival.<sup>7</sup> Mechanical ventilation, noninvasive or via tracheostomy, is able to prevent or reverse ventilatory failure for patients with ALS or other neuromuscular diseases.<sup>8</sup> More attention now needs to be paid to clearing airway secretions.

Assisted coughing techniques, both manual and mechanical, can increase PCF over unassisted levels and, thus, increase airway clearance capacity.<sup>9</sup> Manually assisted coughing requires patient and caregiver cooperation and involves the use of an abdominal thrust following attainment of lung volumes approaching the maximum insufflation capacity (MIC). This is achieved by using a manual resuscitator or a portable volume ventilator to “stack” volumes of air into the lungs, holding them with a closed glottis.<sup>10</sup> Greater PCF reached with assisted coughing can avert respiratory failure and, ultimately, delay or eliminate the need for tracheotomy for airway secretion removal.

Mechanical insufflation-exsufflation (MI-E) is a method for mechanically assisted coughing. MI-E involves a deep insufflation by a positive pressure blower followed immediately by a forced exsufflation in which high expiratory flow rates and a high expiratory pressure gradient are generated between the mouth and the alveoli. If the expiratory flow rates reached with MI-E can exceed those that can be produced during unassisted coughing and, in particular, exceed 2.7 L/s for patients with advanced neuromuscular ventilatory insufficiency,<sup>11</sup> the risk of pulmonary complications can be diminished. While this has been demonstrated for patients with neuromuscular diseases with bulbar muscle function,<sup>5</sup> it has not been demonstrated for bulbar ALS patients. Likewise, intubation, bronchoscopy, and tracheotomy for airway secretion expulsion may be avoided. The aim of this study, which constitutes a part of long-term prospective project whose objective is to evaluate the utility of noninvasive therapeutic procedures in ALS patients, is to determine under what circumstances MI-E is able to generate effective expiratory flow rates for medically stable patients with bulbar and nonbulbar ALS.

Twenty-six consecutively referred patients with ALS without antecedent lung disease or significant kyphoscoliosis (Cobb angle > 70°) were studied. The diagnosis of ALS was established by El Escorial criteria.<sup>12</sup> Videofluoroscopy was performed of the upper airways, the capacity to perform a Valsalva maneuver was determined, and the presence of drooling or articulation difficulties was surveyed in order to estimate bulbar impairment.<sup>13</sup> Bulbar dysfunction was considered when at least one of the previous alterations were present.<sup>13</sup> Exclusion criteria were antecedent barotrauma, pulmonary bullae, or FEV<sub>1</sub>/FVC < 70%. Informed consent was obtained from each subject who took part in the study. All subjects were medically stable for at least 1 month. All measurements were made while the subjects were seated. Spirometry was performed (MS 2000; C. Schatzman; Madrid, Spain) using a mouthpiece and a nose clip. FVC, FEV<sub>1</sub>, and FVE<sub>1</sub>/FVC were recorded in accordance with European Respiratory Society guidelines and suggested normal values.<sup>14</sup>

Maximum inspiratory pressure (P<sub>Imax</sub>) and maximum expiratory pressure (P<sub>E<sub>max</sub></sub>) at the mouth were measured (Electrometer 78.905A; Hewlett-Packard; Andover, MA) with cheek held. P<sub>Imax</sub> was performed close to residual volume and P<sub>E<sub>max</sub></sub> was performed close to total lung capacity, and the pressures sustained for 1 s were observed. Three measurements with < 5% variability were recorded, and the highest value was used for the data analysis. Reference values were those of Morales et al.<sup>15</sup>

PCF were measured using a sealed oronasal mask (King Mask; King System; Noblesville, IN) connected to a pneumotachograph spirometer (MS 2000; C. Schatzman) when the subjects performed a maximal cough effort after a deep inspiration. MIC was attained using a manual resuscitator (Revivator; Hersill; Madrid, Spain) via a sealed oronasal mask (King Mask; King System). The lungs were insufflated to the highest volume that could be held with a closed glottis. The patient was then asked to cough forcefully while a thoracoabdominal thrust was applied. The cough volume and the PCF attained with the MIC (PCF<sub>MIC</sub>) were measured with a pneumotachograph connected to the mask and the manual resuscitator.

The MI-E (Cough-Assist; JH Emerson; Cambridge, MA) was applied through a full face mask (King Mask; King System). It was set at 40 cm H<sub>2</sub>O of insufflation pressure, - 40 cm H<sub>2</sub>O of exsufflation pressure with an insufflation/exsufflation ratio of 2/3, and a pause of 1 s between each cycle.<sup>7,22</sup> The patient was asked to try to keep his airway open but to otherwise remain passive and let the Cough-Assist device act unimpeded on the airways. A thoracoabdominal thrust was applied during exsufflation to further increase the PCF.<sup>9</sup> With a pneumotachograph placed between the mask and the MI-E circuit, PCF generated by MI-E (PCF<sub>MI-E</sub>) was measured.

#### Statistical Analysis

Data were expressed as mean ± SD. Data comparisons were performed by Student's paired and unpaired *t* tests. When the variables did not have a normal distribution, the Mann Whitney test and Wilcoxon test for paired data were used. Receiver operating characteristic (ROC) curves were used in order to identify variables that would best predict those ALS patients for whom MI-E would probably be ineffective (PCF<sub>MI-E</sub> < 2.7 L/s)<sup>4</sup> and those in whom manually assisted coughing would reach greater PCF than MI-E. The level for statistical significance was taken as *p* < 0.05.

## RESULTS

Data for age, sex, pulmonary function, and cough capacity are shown in Table 1. No differences were found between nonbulbar and bulbar patients over the period of time since ALS symptom onset ( $24.75 \pm 12.91$  months vs  $30.70 \pm 18.28$  months,  $p =$  not significant), and in time from establishment of the diagnosis ( $18.44 \pm 13.33$  months vs  $21.70 \pm 16.34$  months,  $p =$  not significant). Statistical differences ( $p < 0.05$ ) were found in lung function and cough capacity parameters between bulbar and nonbulbar patients (Table 1).

Twenty-four patients (92.31%) had MIC greater than FVC (MIC vs FVC,  $p < 0.01$ ). Two patients who could not close their glottises had MIC values equal to FVC ( $1.11 \pm 0.62$  L) [mean  $\pm$  SD]. Both of them also had severe bulbar dysfunction. All the patients with some degree of bulbar dysfunction and MIC greater than FVC were able to obtain a PCFMIC  $> 2.7$  L/s except for one patient (FVC, 0.60 L; MIC, 1.01 L; PCF, 1.87 L/s; PCFMIC, 1.91 L/s). This patient (stable clinically but who had rejected tracheostomy as a means to clear secretions if needed) was probably able to close the glottis enough to increase the MIC, but his expiratory muscles were too weak (PEmax 35.5% of predicted value) to generate an adequate PCFMIC.

Seven patients had PCF  $< 2.7$  L/s ( $2.25 \pm 0.34$  L/s), all of them with bulbar dysfunction. All of them had rejected tracheostomy as mean to clear secretions and/or mechanical ventilation if needed. Comparing these patients (PCF  $< 2.7$  L/s) with those with PCF  $\geq 2.7$  L/s, we found that they presented lower PCFMIC ( $2.80 \pm 0.30$  L/s vs  $5.95 \pm 2.24$  L/s,

$p < 0.001$ ) and PCFMI-E ( $2.79 \pm 0.38$  L/s vs  $4.12 \pm 0.80$  L/s,  $p < 0.001$ ).

MI-E was able to generate PCFMI-E  $> 2.7$  L/s in all but four patients ( $2.55 \pm 0.09$  L/s). A ROC curve was performed in order to seek variables that might predict the patients in whom the MI-E would be ineffective (PCFMI-E  $< 2.7$  L/s). Of all the analyzed variables, PCFMIC had the greatest ( $p < 0.05$ ) area under the curve (0.98;  $p < 0.01$ ; 95% confidence interval, 0.82 to 0.99). A value of 2.7 L/s as cutoff point for the PCFMIC had a sensitivity of 1.00 and a specificity of 0.95 in identifying those patients with ineffective PCFMI-E for mucus clearance ( $< 2.7$  L/s), with a positive predictive value of 0.79 and negative predictive value of 1.00. All these four patients have bulbar dysfunction, MIC  $> 1$  L, and PCFMIC  $< 2.7$  L/s.

Statistical differences ( $p < 0.05$ ) were found between patients with PCFMI-E  $> 2.7$  L/s ( $n = 22$ ) and those with PCFMI-E  $< 2.7$  L/s ( $n = 4$ ) in PCF ( $4.85 \pm 2.32$  L/s vs  $2.18 \pm 0.45$  L/s), PCFMIC ( $5.60 \pm 2.26$  L/s vs  $2.29 \pm 0.40$  L/s), PCFMI-E ( $3.97 \pm 0.82$  L/s vs  $2.55 \pm 0.01$  L/s), and PEmax ( $108.20 \pm 70.21$  cm H<sub>2</sub>O vs  $60.75 \pm 10.90$  cm H<sub>2</sub>O).

A ROC curve was used in the patients we studied in order to seek variables that might predict medically stable patients for whom PCFMIC would be greater than PCFMI-E. The PCFMIC had the greatest area under the curve (0.90;  $p < 0.01$ ; 95% confidence interval, 0.71 to 0.98). A value of 4 L/s as cutoff point for the PCFMIC had a sensitivity of 0.89 and a specificity of 0.75 in identifying patients with PCFMIC greater than PCF, with a positive predictive value of 0.68 and a negative predictive value of 0.93.

**Table 1—Lung Function and Cough Capacity Parameters in the Subjects\***

Variables	Total Population (n = 26)	Nonbulbar (n = 11)	Bulbar (n = 15)
Male/female gender, No.	14/12	7/4	7/8
Age, yr	60.96 $\pm$ 9.34	59.45 $\pm$ 9.62	62.07 $\pm$ 9.30
BMI	26.24 $\pm$ 3.97	28.73 $\pm$ 2.97	24.41 $\pm$ 3.66†
FVC, L	2.02 $\pm$ 1.07	2.58 $\pm$ 1.24	1.62 $\pm$ 0.74†
FVC % predicted	60.27 $\pm$ 25.36	74.91 $\pm$ 26.69	49.53 $\pm$ 18.65†
MIC, L	2.39 $\pm$ 1.07	3.02 $\pm$ 1.22	1.97 $\pm$ 0.75†
PCF, L/s	4.47 $\pm$ 2.31	5.91 $\pm$ 2.55	3.42 $\pm$ 1.44†
PCFMIC, L/s	5.07 $\pm$ 2.41	6.68 $\pm$ 2.71	4.00 $\pm$ 1.48†
PCFMI-E, L/s	3.75 $\pm$ 0.92	4.34 $\pm$ 0.82	3.35 $\pm$ 0.77†
FEV <sub>1</sub> , L	1.84 $\pm$ 0.98	2.26 $\pm$ 1.18	1.54 $\pm$ 0.69†
FEV <sub>1</sub> % predicted	67.08 $\pm$ 27.03	82.45 $\pm$ 28.77	55.80 $\pm$ 19.80†
FEV <sub>1</sub> /FVC	88.39 $\pm$ 9.33	87.34 $\pm$ 8.01	89.17 $\pm$ 10.41
P <sub>imax</sub> , cm H <sub>2</sub> O	- 65.56 $\pm$ 43.77	- 93.45 $\pm$ 47.47	- 43.64 $\pm$ 25.07†
P <sub>imax</sub> % predicted	62.69 $\pm$ 36.60	84.16 $\pm$ 35.41	45.83 $\pm$ 28.50†
PEmax, cm H <sub>2</sub> O	100.96 $\pm$ 65.13	140.45 $\pm$ 75.98	69.93 $\pm$ 32.14†
PEmax % predicted	62.28 $\pm$ 32.91	82.70 $\pm$ 35.47	46.24 $\pm$ 20.04†

\*Data are presented as mean  $\pm$  SD unless otherwise indicated. BMI = body mass index.

† $p < 0.05$  comparing nonbulbar with bulbar group.

All the patients with no clinically relevant impairment in cough capacity ( $PCF \geq 4.5$  L/s)<sup>5</sup> [ $n = 11$ ,  $PCF$ ,  $6.45 \pm 2.12$  L/s; 4 patients with some degree of bulbar dysfunction] had MIC greater than FVC ( $3.13 \pm 1.16$  L vs  $2.84 \pm 1.16$  L,  $p < 0.01$ ). Moreover, in these patients PCFMIC was greater than PCFMI-E ( $7.01 \pm 2.29$  L/s vs  $4.31 \pm 0.92$  L/s,  $p < 0.01$ ).

## DISCUSSION

The most important findings in this study are the usefulness of the MI-E in ALS patients, both bulbar and nonbulbar, the critical role played by the upper airway in the generation of an effective mechanically assisted PCF, and the inability of MI-E to generate greater PCF than those attainable by manually assisted coughing alone for those medically stable patients with milder respiratory dysfunction. In these patients, we can assume that those with  $PCFMIC > 4$  L/s may be unable to generate greater cough flows with the MI-E than manually assisted coughing. This work also demonstrates that inability to close the glottis and airway collapse are distinct factors in determining PCF and the potential effectiveness of MI-E.

Impaired cough capacity is a progressive state found in patients with ALS. The different degree of the involvement in the respiratory and bulbar muscles determines the success of the different assisted-coughing techniques in order to generate an effective PCF to remove airway secretions. Inspiratory muscle weakness produces a diminution of vital capacity and lung recoil pressures, expiratory muscle weakness produces a reduction in the intrathoracic pressure generated during the cough maneuver, and severe bulbar dysfunction with failure to close the glottis reduces or eliminates MIC, decreasing potential lung recoil for an effective cough. The result is a decreased PCF, more evident in bulbar patients, as our findings show. We also found that in those patients with ALS and expiratory and inspiratory muscle weakness but effective bulbar muscles, in order to close the glottis (MIC greater than FVC), the generated PCF with manually assisted coughing is greater than unassisted PCF ( $p < 0.01$ ). This can change an ineffective cough into an effective one.<sup>10,16</sup> Indeed, the findings of our study show that in those patients with ALS and milder respiratory dysfunction and effective bulbar muscles, the generated PCFMIC is greater than those reached with MI-E. In this way, patients with MIC greater than FVC and  $PCFMIC > 4$  L/s present PCFMIC greater than PCFMI-E in a stable condition. However, our results do not show what may happen to these same patients in an acute respiratory illness when they have airway secretions—for instance a pulmonary infection—when

PCFMI-E would be more effective, and thereby more useful, than PCFMIC in order to airway secretions removal.<sup>17</sup> Moreover, this study was conducted applying MI-E with a thoracoabdominal thrust and without any patient cough effort because we wanted to evaluate the peak expiratory flow rates generated by MI-E without patient cooperation. We performed our study thus because it is possible that in very advanced ALS or in situations in which no cooperation will be produced, no cough attempts will be made.<sup>17</sup> However, the patient cough effort, a thoracoabdominal thrust during the exsufflation cycle, and probably greater set pressures in the MI-E will increase the PCFMI-E.<sup>9,18,19</sup>

When manually assisted coughing techniques are unable to generate an effective PCF or when the patient is unable to cooperate, the MI-E is the most effective alternative for generating optimal PCF and eliminating airway secretions.<sup>9</sup> In this way, the values of PCFMI-E recorded in our study are similar to those attained in previous clinical<sup>18,20,21</sup> and experimental studies.<sup>22</sup> The findings of our study show that MI-E is able to generate a  $PCF > 2.7$  L/s in patients with ALS when it is applied via a full face mask for patients both with and without bulbar dysfunction, except for those with severe bulbar dysfunction,  $MIC > 1$  L, and  $PCFMIC < 2.7$  L/s. This fact ( $MIC > 1$  L and manually assisted  $PCF < 2.7$  L/s) means that there is an alteration in the upper airway such as greater instability and weakness these muscles due to bulbar dysfunction.<sup>23</sup> Because of a suspected upper airway collapse during the application of negative pressure, an upper airway CT scan was performed (Dr. M. A. Moya) at baseline and during the exsufflation cycle of MI-E for a patient whose PCFMI-E was  $< 2.7$  L/s (PCFMI-E of 2.55 L/s), and for another patient with bulbar dysfunction and  $PCFMI-E > 2.7$  L/s (PCFMI-E of 3 L/s), and for a nonbulbar patient with  $PCFMI-E > 2.7$  L/s (PCFMI-E of 5.27 L/s). The upper airway CT scans of the three patients showed exsufflation cycle closing of the nasopharynx, with retraction of the uvula, and reduction of the lateral diameter of the pharynx. This narrowing was greatest at the oropharynx (Fig 1, 2). In the patient with  $PCFMI-E < 2.7$  L/s, the maximum reduction of the diameter of the pharynx was 77%; in the patient with bulbar dysfunction and  $PCFMI-E > 2.7$  L/s, it was 60%; and in the patient without bulbar impairment and  $PCFMI-E > 2.7$  L/s, it was 45%.

Koulouris et al<sup>24</sup> proposed the application of negative pressure during tidal expiration (NEP) [ $-3$  to  $-5$  cm  $H_2O$ ] in order to assess expiratory flow limitation. The sudden application of a NEP in healthy subjects produces reflex activation of the genioglossus muscle to maintain upper airway patency<sup>25</sup> and prevent decreases in expiratory flow. If greater NEP is applied, the response of the genioglossus muscle reflex will be

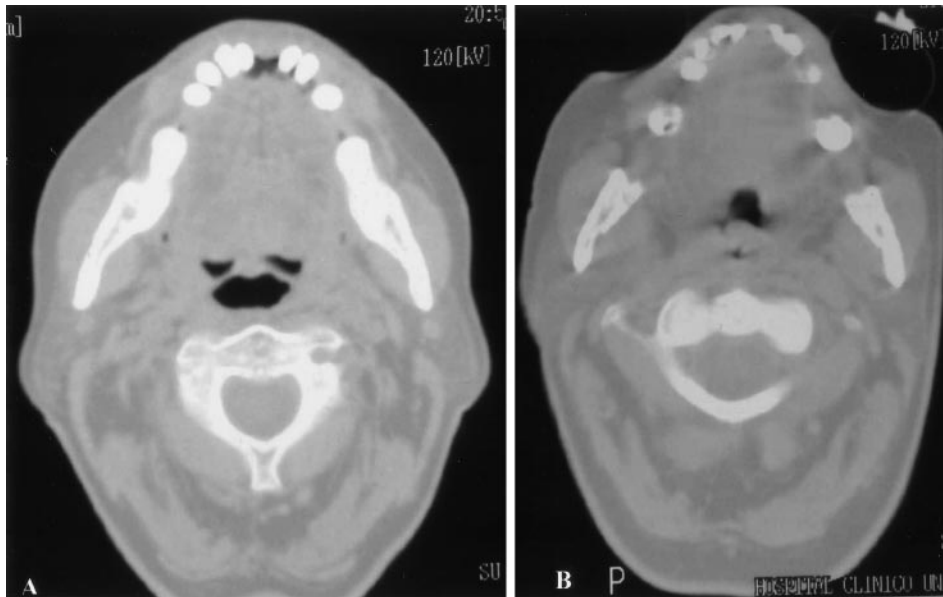


FIGURE 1. Oropharynx CT scan of a bulbar ALS patient with PCFMI-E < 2.7 L/s. *Left, A:* baseline. *Right, B:* during the exsufflation cycle.

greater.<sup>26</sup> Decreases in expiratory flow have also been demonstrated in healthy subjects when a NEP is applied, reflecting a total or partial narrowing of the upper airway, and suggesting some degree of upper airway instability.<sup>27–29</sup> This collapse of the upper airway during the application of NEP that is produced in certain healthy subjects can be due to too long a latency of the pharyngeal dilator muscle reflex or interindividual variations in the sensitivity of the trigger or in the intensity of response.<sup>25</sup> Patients with ALS and impaired bulbar function have weakness of the pharyngeal muscles<sup>13</sup> and, as in other neuromuscular disorders with bulbar dysfunction, the pharyngeal muscles have decreased strength, muscle velocity, and mechanical

power.<sup>30</sup> This fact can produce a diminution of the genioglossus muscle response when a NEP is applied, and produce a narrowing of the upper airway with a decrease in expiratory flows. In this way, the application of the exsufflation cycle of MI-E for those with weakness of genioglossus activity due to bulbar dysfunction would probably produce a dynamic, total, or partial collapse of the upper airway. This can render PCFMI-E ineffective.

The importance of the oropharyngeal musculature has been recognized for the generation of assisted PCF.<sup>16</sup> Our study has permitted the identification of two not mutually exclusive circumstances in the bulbar ALS population: those with failure to close the glottis

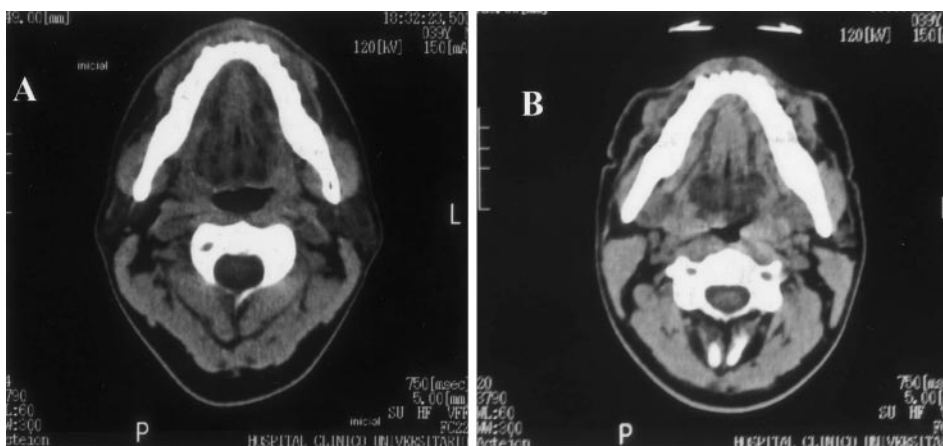


FIGURE 2. Oropharynx CT scan of a nonbulbar ALS patient with PCFMI-E > 2.7 L/s. *Left, A:* baseline. *Right, B:* during the exsufflation cycle.

(MIC equal to FVC, and inability to perform a Valsalva maneuver), in whom manually assisted coughing cannot increase PCF; and those with instability of the pharyngeal walls ( $PCF_{MIC} < 2.7$  L/s and  $MIC > 1$  L), in whom the MI-E is ineffective. One study<sup>7</sup> has found that assisted coughing techniques tend to fail in patients with ALS and severe bulbar dysfunction, and tracheotomy becomes necessary to prolong survival. Moreover, bulbar onset has been related to poor survival.<sup>31</sup> Consequently, we propose periodic monitoring of assisted coughing effectiveness ( $PCF_{MIC}$  and  $PCF_{MI-E}$ ) in order to identify those patients at risk of failure of noninvasive management.

In conclusion, MI-E does not generate greater PCF than manually assisted coughing in those medically stable ALS patients with relatively little lung function impairment ( $PCF_{MIC} > 4$  L/s), but it is able to significantly increase  $PCF > 2.7$  L/s for patients both with and without bulbar dysfunction, except for those with bulbar dysfunction who also have a  $MIC > 1$  L and  $PCF_{MIC} < 2.7$  L/s, probably due to dynamic collapse of the upper airway during the exsufflation cycle.

ACKNOWLEDGMENT: The authors thank Dr. John R. Bach and Dr. Edward A. Oppenheimer for their helpful review of this manuscript.

#### REFERENCES

- Schiffman PL, Blesh JM. Pulmonary function at diagnosis of amyotrophic lateral sclerosis: rate of deterioration. *Chest* 1993; 103:508–513
- Lechtzin N, Wiener CM, Clawson MSN, et al. Hospitalization in amyotrophic lateral sclerosis: causes, costs and outcomes. *Neurology* 2001; 56:753–757
- King M, Brock G, Lundell C. Clearance of mucus by simulated cough. *J Appl Physiol* 1985; 58:1776–1782
- Bach JR, Saporito LR. Criteria for extubation and tracheostomy tube removal for patients with ventilatory failure: a different approach to weaning. *Chest* 1996; 110:1566–1571
- Bach JR, Ishikama Y, Kim H. Prevention of pulmonary morbidity for patients with Duchenne muscular dystrophy. *Chest* 1997; 112:1024–1028
- Poponick JM, Jacobs I, Supinski G, et al. Effect of upper respiratory tract infection in patients with neuromuscular disease. *Am J Respir Crit Care Med* 1997; 156:659–664
- Bach JR. Amyotrophic lateral sclerosis: prolongation of life by noninvasive respiratory aids. *Chest* 2002; 122:92–98
- Bach JR, Alba AS, Saporito LR. Intermittent positive pressure ventilation via the mouth as an alternative to tracheostomy for 257 ventilator users. *Chest* 1993; 103:174–182
- Bach JR. Mechanical insufflation-exsufflation: comparison of peak expiratory flows with manually assisted and unassisted coughing techniques. *Chest* 1993; 104:1553–1562
- Kang SW, Bach JR. Maximum insufflation capacity: vital capacity and cough flows in neuromuscular disease. *Am J Phys Med Rehabil* 2000; 79:222–227
- Bach JR, Smith WH, Michaels J, et al. Airway secretion clearance by mechanical exsufflation for post-poliomyelitis ventilator assisted individual. *Arch Phys Med Rehabil* 1993; 74:170–177
- World Federation of Neurology Research Group on neuromuscular disease, subcommittee on motor neuron disease. El Escorial World Federation on Neurology Criteria for the Diagnosis of Amyotrophic Lateral Sclerosis. *J Neurol Sci* 1994; 124:96–107
- Hadjikitou S, Wiles CM. Respiratory complications related to bulbar dysfunction in motor neuron disease. *Acta Neurol Scand* 2001; 103:207–213
- Quanjer PhD, Tammeling GJ, Cotes JE, et al. Lung volumes and forced ventilatory flows: report of Working Party "Standardization of Lung Function Test." *Eur Respir J* 1993; 6(suppl 16):5–40
- Morales P, Sanchis J, Cordero PJ, et al. Presiones respiratorias estáticas máximas en adultos: valores de referencia en la población caucásica mediterránea. *Arch Bronconeumol* 1997; 33:213–219
- Kang SW, Bach JR. Maximum insufflation capacity. *Chest* 2000; 118:61–65
- Servera E, Sancho J, Gómez-Merino E, et al. Noninvasive management of an acute chest infection for a patient with ALS. *J Neurol Sci* 2003; 209:11–13
- Barach AL, Beck GJ, Bickerman HA, et al. Physical methods simulating mechanism of the human cough. *J Appl Physiol* 1952; 5:85–91
- Braun SR, Giovannoni R, O'Connor M. Improving the cough in patients with spinal cord injury. *Am J Phys Med Rehabil* 1984; 63:1–10
- Chatwin M, Ross E, Hart N, et al. A comparison of the effect of mechanical insufflation-exsufflation, noninvasive ventilation and physiotherapy assistance on peak cough flow in neuromuscular disease. *Thorax* 2001; 56(suppl3):48–49
- Mustfa N, Aiello M, Lyall RA, et al. Cough augmentation in bulbar and non-bulbar motor neuron disease patients [abstract]. *Thorax* 2001; 56(suppl3):49
- Gómez-Merino E, Sancho J, Marín J, et al. Mechanical insufflation-exsufflation: pressure, volume and flow relationships and the adequacy of the manufacturer's guidelines. *Am J Phys Med Rehabil* 2002; 81:579–583
- Bach JR, Tzeng A, Servera E. Ayudas de medicina física en la prevención de morbilidad y mortalidad de los pacientes con enfermedades neuromusculares. In: Giménez M, Servera E, Vergara P, eds. *Prevención y rehabilitación en patología respiratoria crónica*. Madrid, Spain: Panamericana, 2001; 421–430
- Koulouris NG, Valta P, Lavoie A, et al. A simple method to detect expiratory flow limitation during spontaneous breathing. *Eur Respir J* 1995; 8:306–313
- Tantucci C, Mehiri S, Dugnet A, et al. Application of negative expiratory pressure during expiration and activity of genioglossus in humans. *J Appl Physiol* 1998; 84:1076–1082
- Horner RL, Innes JA, Guz A. Reflex pharyngeal dilator muscle activation by stimuli of negative airway pressure in awake man. *Sleep* 1993; 16(suppl):S85–S86
- Suratt PM, Wilhoit SC, Cooper K. Induction of airway collapse with subatmospheric pressure in awake patients with sleep apnea. *J Appl Physiol* 1984; 57:140–146
- Sanna A, Veriter C, Kurtansky A, et al. Contraction and relaxation of upper airway muscles during expiratory application of negative pressure at the mouth. *Sleep* 1994; 17:220–225
- Younes M, Sani R, Patrick W, et al. An approach to the study of upper airway function in humans. *J Appl Physiol* 1994; 77:1383–1392
- Attal P, Lambert F, Marchand-Adam S, et al. Severe mechanical dysfunction in pharyngeal muscle from adult mdx mice. *Am J Respir Crit Care Med* 2000; 162:278–281
- Magnus T, Beck M, Giess R, et al. Disease progression in amyotrophic lateral sclerosis: predictors of survival. *Muscle Nerve* 2002; 25:709–714

**Efficacy of Mechanical Insufflation-Exsufflation in Medically Stable Patients With Amyotrophic Lateral Sclerosis**

Jesús Sancho, Emilio Servera, Juan Díaz and Julio Marín

*Chest* 2004;125;1400-1405

DOI 10.1378/chest.125.4.1400

**This information is current as of December 9, 2007**

<b>Updated Information &amp; Services</b>	Updated information and services, including high-resolution figures, can be found at: <a href="http://chestjournal.org/cgi/content/full/125/4/1400">http://chestjournal.org/cgi/content/full/125/4/1400</a>
<b>References</b>	This article cites 28 articles, 14 of which you can access for free at: <a href="http://chestjournal.org/cgi/content/full/125/4/1400#BIBL">http://chestjournal.org/cgi/content/full/125/4/1400#BIBL</a>
<b>Citations</b>	This article has been cited by 1 HighWire-hosted articles: <a href="http://chestjournal.org/cgi/content/full/125/4/1400">http://chestjournal.org/cgi/content/full/125/4/1400</a>
<b>Permissions &amp; Licensing</b>	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: <a href="http://chestjournal.org/misc/reprints.shtml">http://chestjournal.org/misc/reprints.shtml</a>
<b>Reprints</b>	Information about ordering reprints can be found online: <a href="http://chestjournal.org/misc/reprints.shtml">http://chestjournal.org/misc/reprints.shtml</a>
<b>Email alerting service</b>	Receive free email alerts when new articles cite this article sign up in the box at the top right corner of the online article.
<b>Images in PowerPoint format</b>	Figures that appear in CHEST articles can be downloaded for teaching purposes in PowerPoint slide format. See any online article figure for directions.

A M E R I C A N C O L L E G E O F



P H Y S I C I A N S<sup>®</sup>