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0894-9115/02/8107-0506/0
American Journal of Physical Medicine & Rehabilitation

Research Article

Peak Flow and Peak Cough Flow in the Evaluation of Expiratory Muscle Weakness and Bulbar Impairment in Patients with Neuromuscular Disease

ABSTRACT

Suárez AA, Pessolano FA, Monteiro SG, Ferreyra G, Capria ME, Mesa L, Dubrovsky A, De Vito EL: Peak flow and peak cough flow in the evaluation of expiratory muscle weakness and bulbar impairment in patients with neuromuscular diseases. *Am J Phys Med Rehabil* 2002;81:506–511.

Objective: To study the expiratory muscle force and the ability to cough estimated by the peak expiratory flow and peak cough flow in patients with Duchenne muscular dystrophy and amyotrophic lateral sclerosis.

Design: A total of 27 patients with amyotrophic lateral sclerosis and 52 patients with Duchenne muscular dystrophy were studied. From the group of 144 normal subjects of this laboratory, we selected 38 for comparison.

Results: The maximal inspiratory pressure in patients with Duchenne muscular dystrophy and amyotrophic lateral sclerosis was 64.5 ± 24.7% and 37.8 ± 21.8%, respectively, and maximal expiratory pressure was 64.2 ± 32.5% and 37.7 ± 21.6%, respectively. Patient groups showed a significant lower peak expiratory flow than normal subjects. Higher peak cough flow than peak expiratory flow was found in all groups. The peak cough flow–peak expiratory flow difference was 46 ± 18% in normal subjects, 43 ± 23% in patients with Duchenne muscular dystrophy, and 11 ± 17% in patients with amyotrophic lateral sclerosis. The peak expiratory flow and peak cough flow were not different in bulbar onset amyotrophic lateral sclerosis. In patient groups, the dynamic and static behavior correlated positively.

Conclusions: These results suggest that peak cough flow–peak expiratory flow is useful to monitor expiratory muscle weakness and bulbar involvement and to assess its evolution in these patients.

Key Words: Flow Rate, Peak Expiratory, Cough, Duchenne Muscular Dystrophy, Amyotrophic Lateral Sclerosis, Neuromuscular Diseases, Expiratory Muscle Weakness

Weakness of expiratory muscles is a common and prominent finding in patients with neuromuscular diseases and respiratory involvement. Bronchial mucus retention, atelectasis, and infection are well known deleterious effects of inefficient cough. For these reasons, the evaluation of expiratory muscles force is important in these patients. It may be assessed measuring the maximal expiratory pressure (MEP) performed against an occluded airway after a full inspiration.[1] This maneuver is usually extremely difficult to perform in patients with severe weakness of facial muscles. An acceptable alternative is the peak flow (PF) determination, which, in absence of bronchial obstruction, reflects the expiratory muscle force. Thereby, PF and peak cough flow (PCF) are easier to measure than MEP in patients with bulbar weakness.

Respiratory muscle weakness in Duchenne muscular dystrophy (DMD) is the main factor leading to respiratory failure.[2] In addition to the expiratory muscle weakness, bulbar muscle impairment, such as in amyotrophic lateral sclerosis (ALS),[3] provokes inefficient glottis closure with inadequate upper airway protection, leading to aspiration of food or saliva.

The maximal expiratory flow values during a cough maneuver (PCF) are greater than the classical PF. This fact implies an appropriate bulbar function (firm glottis closure) that allows generating high thoracoabdominal pressure and expiratory flows.[4] It is expected that the impaired bulbar function diminishes PCF-PF difference. This difference could be used as an objective measurement of bulbar involvement and its evolution in several neuromuscular diseases. The purpose of this study was to compare expiratory muscle force and the ability to cough, estimated by the maximal expiratory flow during a cough maneuver, in a population of patients with ALS and children with DMD.

MATERIALS AND METHODS

A total of 27 patients with ALS patients were enrolled in this study. The diagnosis of ALS was established according to the El Escorial guidelines;[5] all the patients were included in the category of definite or probable. Patients were divided in bulbar ($n = 7$) or spinal ($n = 20$) onset, according with the appearance of their first symptoms.

In 4 of the 27 patients with ALS (17 male patients), more than one study (two to five determinations) was carried out within 13.7 ± 8.9 mo (range, 5–26 mo). A total of 36 PF-PCF–paired determinations were performed.

A total of 52 patients with a diagnosis of DMD were studied. The diagnosis was established by clinical criteria and confirmed by dystrophin immunostaining. The motor functional capacity, according to the classification of Vignos et al.[6] (score, 1–10) was used (score 1, the patient walks and climbs stairs without assistance; score 10, the patient is in a wheelchair or bed, elbow flexors less than antigravity). A total of 24 patients received deflazacort treatment (0.5–1 mg/kg). In 4 of 52 patients with DMD, more than one study (two to three determinations) was performed. A total of 57 PF-PCF–paired determinations were carried out.

A total of 144 normal subjects, nonsmokers, asymptomatic, non–medical personnel were studied. Forty-six normal subjects were excluded because of a PCF of >800 liters/min (upper limit of the PF meter). The patients performed standard spirometric tests (Compact II, Vitalograph, Buckingham, U.K.). Maximal inspiratory pressure and MEP (Validyne MP 45, Validyne Engineering, Northridge, CA) were performed with a mouthpiece with lipseal. Conventional PF and PCF were obtained with a PF meter (Personal Best, normal or low range). The institutional review board for human study approved the protocol of this study. All subjects and their parents were informed about its nature, and appropriate consent was obtained.

Signal Processing. Maximal inspiratory pressures and MEP were displayed on a four-channel polygraph pen recorder (Physiograph MK-IV-P) and stored in a magnetic tape pulse-code-modulation digital recording adapter (Vetter Digital 4000 A). The signals were passed for acquisition through a 16 bit analog to digital conversion board (Sponge Inc., Data Translation) at a sampling rate of 60 Hz and stored in a personal computer for future off-line analysis. The signal analysis was carried out with a software (Start IS, Canada).

Statistical Analysis. Data mean values are followed by standard deviation of the mean. After testing normal distribution (Kolmogorov-Smirnov test), we chose Wilcoxon's signed-rank test to assess differences between PF and PCF in the same subject. Mann-Whitney rank-sum test was used to test differences between groups (SigmaStat 2.0, Jandel Scientific Software, San Rafael, CA). Slopes were determined by linear regression analysis. Differences with $P < 0.01$ were considered significant. Normal values of respiratory pressures were taken from Stefanuti and Fitting[7] and Rochester and Arora.[8]

RESULTS

At the time of this study, patients with ALS exhibited a wide range of neurologic deficits. Limb muscle weakness of a single extremity to generalized muscle weakness with bulbar involvement was observed. Fifty percent of the patients were wheelchair users. At the time of the study, 66% of patients with spinal onset had bulbar impairment. The es-

timated duration of disease was 44.1 ± 30.4 mo.

By definition, glottic closure is necessary for a cough. As the bulbar muscle weakness worsens, cough flows eventually fail to exceed PF. When they do not exceed peak expiratory flows, it is because of partial or total inability to close the glottis. Therefore, in some patients with ALS with complete inability to close the glottis, the PCFs are really only PFs. The mean motor functional capacity in patients with DMD was 5.7 ± 3.2. Fifty-six percent of the 52 children with DMD were ambulatory (functional scale, 1–7), and the remaining were confined to a wheelchair (functional scale, 8–10). Our normal group was composed of 98 subjects (34 male subjects), the mean age was 34 ± 15 yr, mean body weight was 64 ± 14 kg, and mean height was 166 ± 8 cm. The PF and PCF values were 481 ± 76 and 692 ± 67, respectively ($P < 0.001$). The PCF-PF difference (percentage of PF) was 46 ± 18%.

The maximal inspiratory pressure in patients with DMD and ALS was 61.5 ± 21.5 and 43.5 ± 32.5 cm H_2O, respectively; MEP was 72.1 ± 31.9 and 67.8 ± 48.4 cm H_2O, respectively. Table 1 lists the physical characteristics, the forced vital capacity, and the maximal static respiratory pressures (percentage of normal values) in patients with DMD and ALS. Thoracic-pulmonary restriction and respiratory muscle weakness were the prominent findings.

To perform PF comparisons with patients with ALS and DMD, 38 normal subjects (23 male subjects) were selected (mean age, 37 ± 20 yr; body weight, 68 ± 14 kg; height, 168 ± 9 cm) and divided in two groups. The PF and PCF values (liters per minute) in normal subjects, patients with DMD, and patients with ALS are shown in Table 2. Both patient groups showed a significantly lower PF than normal subjects ($P < 0.001$). In all groups, PCF was higher than PF ($P < 0.001$). As a whole, patients with ALS showed a significantly lower PCF-PF difference (in percentage of PF) when compared with the normal and DMD group ($P < 0.001$).

TABLE 1

Physical characteristics and respiratory test in patients with Duchenne muscular distrophy (DMD) and amyotrophic lateral sclerosis (ALS)

	DMD	ALS
Age (yr)	13 ± 5	55 ± 13
Height (cm)	135 ± 16	168 ± 9
Weight (kg)	37.7 ± 20.8	63.6 ± 17.5
FVC (% normal value)	70.5 ± 34.6	45.8 ± 26.9
MIP (% normal value)	64.5 ± 24.7	37.8 ± 21.8
MEP (% normal value)	64.2 ± 32.5	37.7 ± 21.6

FVC, forced vital capacity; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure.

The relationships between PF and PCF in normal subjects, patients with DMD, and patients with ALS (related to identity line) are shown in Figure 1. Lower PF values are observed in patients with DMD and ALS. All normal subjects and patients with DMD showed PCF values higher than PF. In patients with DMD, no relationship was found between PCF-PF difference and age ($r = 0.188$, $P = 0.16$). No differences between PF and PCF were observed in most patients with ALS. All patients with ALS with bulbar onset were unable to increase the flow rate values during the cough maneuver.

Time-dependent changes in the PF and PCF in two patients with ALS are shown in Figure 2. Decreases in the flow rates and in the difference between PCF and PF were observed, reflecting increasing muscle respiratory weakness and bulbar impairment.

The relationship between dynamic (PF) and static (MEP) behavior of the expiratory muscles in patients with DMD and ALS is shown in Figure 3. As expected, both variables were directly related ($P < 0.001$). The equation PF = 49.62 + 2.27 × MEP, enabled us to predict the PF values, starting from MEP. The determina-

TABLE 2

Peak flow (PF) and the peak cough flow (PCF) values (liters/min) in normal subjects, patients with Duchenne muscular distrophy (DMD), and patients with Amyotrophic Lateral Sclerosis (ALS)

	Normal ($n = 12$)	DMD ($n = 57$)	Normal ($n = 26$)	ALS ($n = 36$)
Age (yr)	15 ± 2	13 ± 5[a]	47 ± 16	55 ± 13[a]
PF	504 ± 72	207 ± 78[b]	492 ± 73	181 ± 144[b]
Peak Cough Flow	720 ± 64[c]	294 ± 124[c]	695 ± 70[c]	213 ± 193[c]
Difference PCF-PF (% PF)	44 ± 16	43 ± 23	43 ± 13	11 ± 17[d]

n, number of paired determination.
[a]Not significant with respective normal.
[b]$P < 0.001$ with respective normal.
[c]$P < 0.001$ with the paired PF.
[d]$P < 0.001$ with normal and DMD.

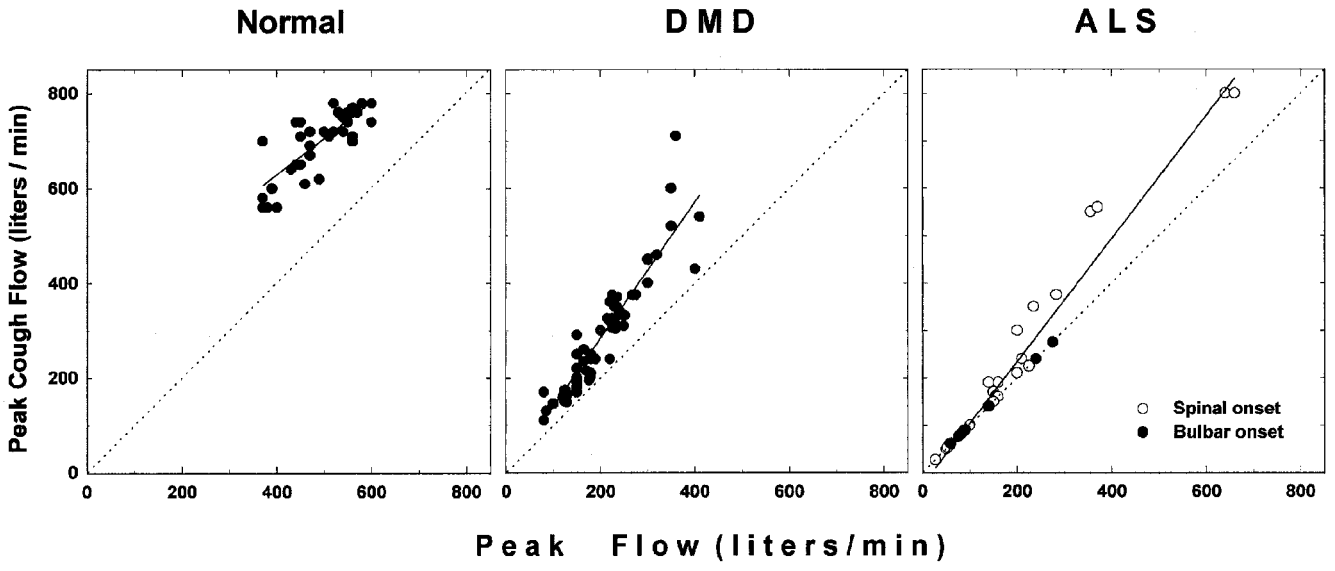

Figure 1: Identity lines between peak cough flow and peak flow values (liters per minute) in normal subjects, patients with Duchenne muscular dystrophy (*DMD*), and patients with amyotrophic lateral sclerosis (*ALS*). Lower peak flow values are observed in patients with DMD and ALS. No differences between peak cough flow and peak flow were observed in most of the patients with ALS. *Closed circles* (in the identity line) show the ALS patients with bulbar onset.

tion coefficient (0.58) explain that about 58% of PF changes are caused by MEP changes. The regression coefficient for MEP *vs.* PF in patients with ALS was 0.84 ($P < 0.01$), whereas the value was 0.59 ($P < 0.01$) in patients with DMD.

DISCUSSION

A cough is a physiologic mechanism that protects the lung from the inhalation of foreign materials and clears excessive bronchial and other secretions. Weakness of inspiratory muscles prevents reaching high lung volumes and decreases the cough effectiveness by putting the expiratory muscles at a mechanical disadvantage. This is a frequent finding in the heterogeneous group of neuromuscular diseases.

During the cough compressive phase, in contrast with the usual forced vital capacity maneuver, the glottis is closed by contraction of the adductor muscles of the arytenoid cartilages. The expiratory muscles contract against the closed glottis, causing a rapid rise in the intraabdominal and intrathoracic pressures, which reach values 30–180% greater than those observed during forced expiratory maneuvers at the same lung volumes.[4] As expected, the maximal expiratory cough flow rate is greater. Supporting the hard palate with the tongue is another gas-compressing mechanism observed in some subjects. Several nerves intervene in the mechanism of the cough, such as vagus, glossopharyngeal, phrenic, trigeminal, facial, hypoglossal, and accessory nerves. Some of them are involved in the glottis closure.

The PF and PCF are easier to measure than MEP in patients with bulbar weakness. However, we obtained reliable measurements of MEP by using a mouthpiece with lipseal, and in addition, the mouth leaks were suppressed by a technician holding the lips.

The patients with DMD showed expiratory muscle weakness (measured in terms of MEP and PF). The difference between the PCF and PF maneuvers, 43 ± 23%, was similar to that observed in the normal subjects (Table 2). These patients can develop bulbar muscle dysfunction so that the ratio PCF-PF/PF may very well decrease with age and advancing weakness, although, of course, their bulbar muscle involvement is rarely, if ever, as severely affected as that for patients with advanced bulbar ALS. In the patients with DMD, the PCF-PF difference not decrease with age.

Kang and Bach[9] studied, in 108 patients with several neuromuscular diseases (32 patients with DMD and 30 patients with ALS), the relationship between forced vital capacity, maximum insufflation capacity, and both unassisted and assisted PCF. The group whose maximum insufflation capacity was greater than their forced vital capacity showed significant increases in the PCF. Patients with both greater unassisted or assisted PCF are able to expel airway mucus and avert respiratory complications.

We believe that the PCF is related to an appropriate bulbar function (firm glottis closure). Bulbar muscle compromise, present in patients with ALS, impairs the proper glottis closure and upper airway protection, leading to an ineffective cough. Our results confirm this belief.

In our patients with ALS, other than expiratory muscle weakness, the

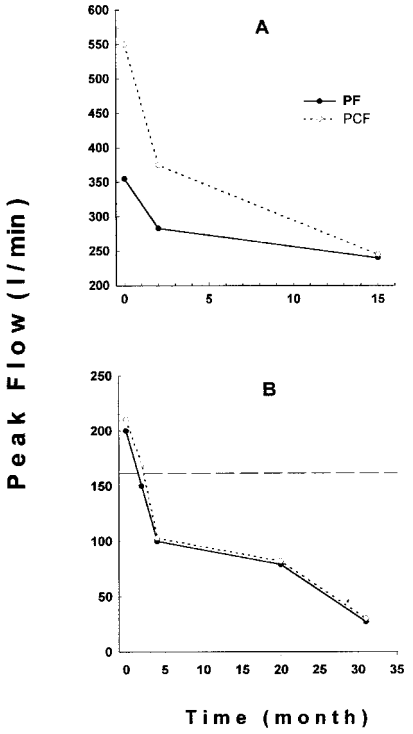

Figure 2: Changes in peak flow (*PF*) and peak cough flow (*PCF*) in two patients with amyotrophic lateral sclerosis. The *first point* represents the time of the first evaluation. Patient 1 (*A*) shows decreases in both the PF and the PCF-PF difference, reflecting expiratory muscle weakness and progressive bulbar function impairment, respectively. Patient 2 (*B*) shows an early PCF-PF narrowing and progressive decrease in the flow rates. The *horizontal dotted line* indicates PCF equal to 160 liters/min. Lower values are associated with an ineffective cough.

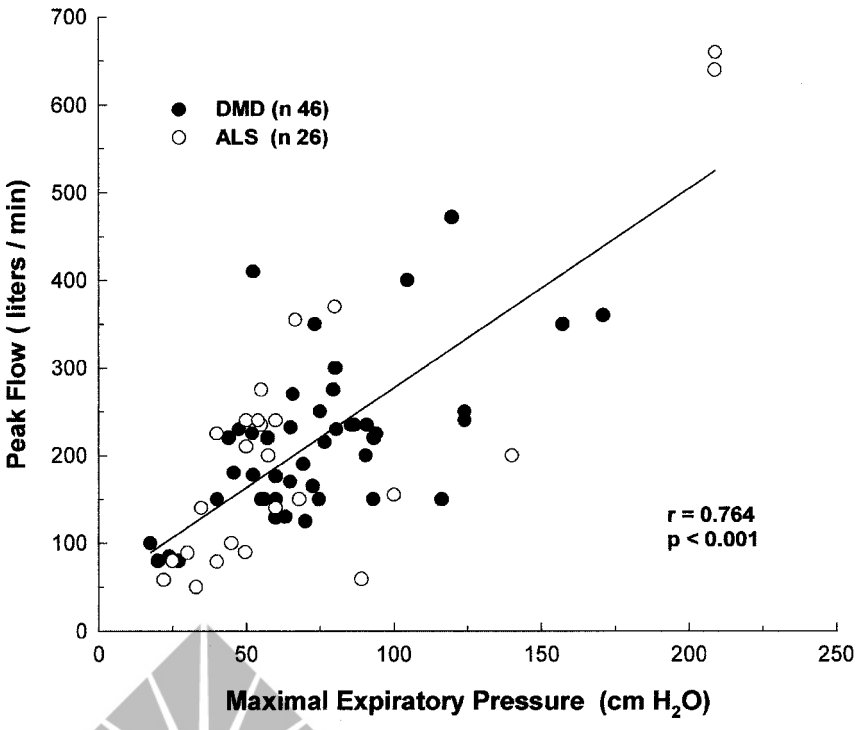

Figure 3: Relationship between peak flow and maximal expiratory pressure in patients with Duchenne muscular dystrophy (*DMD*) and amyotrophic lateral sclerosis (*ALS*). The relationship between dynamic (peak flow) and static (maximal expiratory pressure) behavior of the expiratory muscles in patients with DMD and ALS is shown. Both variables were directly related.

PCF-PF difference (in percentage of PF) was 11 ± 17%, a lower value than that obtained in the normal and DMD group. All of the patients with bulbar onset ALS were unable to increase the flow rate values during the cough maneuver (Fig. 1). Progressive expiratory muscle weakness added to bulbar involvement was a common finding in the evolution of patients with ALS (Fig. 2). It is evident that there will be differences in the PCF and PF only if the abdominal muscles are activated during the expiratory maneuver. Theoretically, extreme expiratory muscular weakness may obliterate the PCF-PF difference in patients with an intact glottis. In these patients, the abdominal thrust substitutes for the abdominal (expiratory) muscle weakness, so air stacking and assisted coughing can be more specific for bulbar function. The MEP value in our ALS patients was 67.8 ± 48.4 cm H_2O, so they were able to contract expiratory muscles to generate static pressure. Patients with DMD with similar expiratory muscle weakness (MEP, 72.1 ± 31.9 cm H2O) were able to produce a higher PCF. In patients with severe expiratory muscle weakness, the assisted PCF would likely be a more sensitive indicator of bulbar dysfunction.

In a preliminary report, Lopes et al.[10] explored the relationship between spirometric parameters, maximal respiratory pressures, and PCF measurements in 14 patients with ALS (seven patients with bulbar involvement). The mean PCF value of the patients was 334 ± 146 liters/min. Using regression analysis, they concluded that the ability to generate greater PCF was more dependent on lung volumes (total lung capacity and forced vital capacity, $P < 0.001$) than MEP ($P < 0.05$). Surprisingly, no differences were found between patients with and without bulbar involvement. Bulbar weakness makes MEP difficult to measure accurately and may worsen the correlation between PCF and MEP. The PF is easier to perform that the MEP.

The clinical relevance of the PCF has been defined primarily in patients with neuromuscular ventilatory impairment with endotracheal or tracheostomy tubes.[11] The ability to generate PCF of at least 160 liters/min was necessary for successful extubation or tracheostomy tube decannulation. In absence of bronchial obstruction, the PF evaluates the dynamic performance of the expiratory muscles. MEP is a recognized measure of the strength of the expiratory muscles under static conditions. In patients with DMD and ALS, both variables were correlated as shown in Figure 3.

These results suggest that measuring the PF and PCF difference is useful to monitor expiratory muscle weakness and bulbar involvement and to assess its evolution in these patients.

ACKNOWLEDGMENT

We thank Dr. Aquiles J. Roncoroni for critical review of the manuscript.

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