Reproducibility and responsiveness of a noninvasive EMG technique of the respiratory muscles in COPD patients and in healthy subjects

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Submitted 27 August 2003; accepted in final form 27 November 2003

The aim of the present study was to assess the reproducibility of this EMG technique between test day 1 and test day 2 in both COPD patients and healthy subjects; and 2) to assess the responsiveness (sensitivity to change) of this EMG technique by evaluating and comparing respiratory muscle activity and breathing patterns in patients with COPD (13, 21). Furthermore, we added the Sc, as it is known that these muscles are important in achieving adequate ventilation in patients with COPD (7).

METHODS

Subjects

Seven healthy subjects and seven COPD patients were included. Baseline characteristics are shown in Table 1. COPD was defined according to the American Thoracic Society criteria (1). The COPD patients were diagnosed with chronic obstructive pulmonary disease (COPD) and were included in the study if they had a forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) ratio < 0.7 and a history of smoking. The healthy subjects were non-smokers and did not use any respiratory medication. The study was approved by the local ethics committee, and all subjects gave written informed consent before inclusion in the study. Baseline characteristics are shown in Table 1. COPD was defined according to the American Thoracic Society criteria (1). The COPD patients were diagnosed with chronic obstructive pulmonary disease (COPD) and were included in the study if they had a forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) ratio < 0.7 and a history of smoking. The healthy subjects were non-smokers and did not use any respiratory medication. The study was approved by the local ethics committee, and all subjects gave written informed consent before inclusion in the study.
patients were recruited from the outpatient clinic of the University Hospital Groningen or from the affiliated rehabilitation facility Beatrixoord, Haren. Excluded were patients with other lung diseases than COPD. Patients had to be in a stable condition, without signs or symptoms of an exacerbation in the last 12 mo before the study. Healthy subjects were defined as having a normal pulmonary function (Tiffeneau index >75%).

All participants were informed about the purpose of the study and gave informed consent. The study was approved by the Medical Ethics Committee of the University Hospital Groningen.

**Experimental Protocol**

The EMG recordings were performed twice, on 2 different days, with a time interval from 1 to 4 wk. Electrical muscle activity of the frontal diaphragm (FD), dorsal diaphragm (DD), Int, abdominal muscles (Abd), and Sc was derived during breathing at rest (T0) and during breathing through an inspiratory threshold device (Threshold IMT; Respironics) of 7 (T1), 14 (T2), and 21 (T3) cmH2 O for 2 min each, with 2-min rest between the episodes of breathing through the threshold. During the measurements, the subjects were sitting in a comfortable chair and were asked not to move or talk. During the measurement, the investigator stood at the left of the subjects and held the threshold device.

**EMG Recordings**

The electrical activity of the FD, DD, Int, and left and right Sc was derived transcutaneously from pairs of electrodes (Neotrode, Conmed) placed as follows: one pair bilaterally at the costal margin in the nipple line; one pair bilaterally on the back at the level of the diaphragm; one pair in the second intercostal spaces one electrode left and one right, 3 cm parasternal; and bipolar electrodes left and right on the neck over the Sc. The EMG signals of the rectus abdominis muscle were derived from bipolar electrode pairs: one pair on the right and one pair on the left side, 4 cm apart, at the level of the umbilicus. The common electrode was placed at the level of the sternum. The EMG did not significantly exceed the power of the amplifier and ADC noise was <2 μV at peak power. The AUX channels had an instrumentation amplifier with both common mode and differential signal ranges of 6 V, an input impedance of >1 GΩ, and a common mode rejection range of >100 dB. We utilized the same ADC as that used for the EXG channels but with a least significant bit of 1.43 μV. Each AUX input connector was provided with a symmetrical 10-V, 10-mA power supply for powering analog signal conditioning circuits. Although the maximum f0 of the front-end was 2 kHz, we found that, during tidal breathing, the sensitivity for the detection of respiratory muscle activity was optimal at a f0 of ~400 Hz. At higher sample frequencies, to allow for an increased bandwidth for EMG signals, it appeared that the power of the EMG did not significantly exceed the power of the amplifier and ADC noise in the higher frequency bands. The EXG signal was transformed into an EMG signal by means of a digital first-order, high-pass filter (time constant = 0.01 s), as an electrophysiological signal is characterized by the position of the electrodes in relation to the electrically active tissue and its signal properties. For patient safety, the front-end was isolated from the main supply by a highly isolated power supply, and all signals were sent to a computer via fiber optics. All data processing, recording, postanalysis, and reporting were conducted by the POLY data-acquisition and processing package (Inspector Research Systems, Amsterdam, The Netherlands).

![Fig. 1. Placement of the 2 magnetometer respiration (MR) bands (B1 and B2) and the electrodes. EC, common electrode; E1 and E2, intercostal electrodes; E3 and E4, frontal diaphragm electrodes; E5 and E6, dorsal diaphragmatic electrodes; E7–8 and E9–10, right and left abdominal electrodes, respectively; E11–12 and E13–14, right and left scalene muscle electrodes, respectively.](http://jap.physiology.org/doi/abs/10.1152/jappl.00673.2004)
Substantial heart activity interferes with the diaphragm EMG signals measured at the trunk. The electrical heart activity was removed from the respiratory muscle activity by the following process: the electrical ventricular activity of the heart (QRS) complexes of the electrocardiogram was easily detected and stretched into a pulse with a length of 100 ms. A cut was made in the slightly delayed EMG signal to completely filter out the QRS complex (gated EMG). Next, the gated EMG was rectified and averaged with a moving time window of 200 ms. Finally, the missing signal in the gate was filled with the running average, resulting in a fairly good interpolation during the gate and an almost electrocardiogram-free averaged EMG signal.

**Magnetometer Respiration Monitoring**

Gross changes in depth of breathing were measured by means of magnetometer respiration (MR) bands (Respiband, SensorMedics, Biltzoven, The Netherlands): one placed around the chest and one around the abdomen. The MR bands were connected to and powered by the AUX input. After analog-to-digital conversion, scaling and filtering of the data were performed digitally, transforming the AUX input signal into an independent signal to monitor respiration.

**Data Analysis and Statistics**

To determine the peak and bottom values of the respiratory EMG, we used an inspiration synchronized averager. The chest band signal was used to detect the beginning of an inspiration. The beginning of an inspiration started the collection of samples from the averaged EMG signals in data buffers. Sampling continued until the beginning of the next inspiration was detected. The data in the buffers containing the samples of one inspiration cycle were moved to the interval data buffers, and the collection of EMG data from a new inspiration was started. The data in the interval buffers were resampled to a normalized interval time and summed to averaging buffers (26). To calculate the mean peak-to-peak excursion, 6–10 breathings were averaged. From the average data, the highest and lowest peak were detected for each signal. The differences between the peak and bottom values were reported as the mean peak-to-peak values.

For the analysis of the EMG signals, we used 6–10 successive breaths in the time interval before the first load (T0) and during the three increasing loads (T1, T2, and T3). EMG data were reported as the logarithm of the EMG activity ratio (log EMGAR). A ratio was calculated of the mean peak-to-peak inspiratory activity during the subsequent loads (T1–T3) and the mean peak-to-peak value at baseline (T0). The logarithmic transformation for the EMGAR was used to make the relative change in the EMGAR symmetric around unity.

To obtain an EMG signal representing the whole diaphragm, the mean of the activity of the FD and the DD was used.

Reproducibility of the EMG technique was assessed by comparing the log EMGAR values of the diaphragm, the Int, and the left Sc at the subsequent inspiratory loads at test day 1 with the log EMGAR values at test day 2. To assess the reproducibility of a technique, we compared signals over the full range of signal amplitude (T1, T2, and T3). Pearson’s correlation coefficients and the method described by Bland and Altman (4) were used to assess reproducibility.

Responsiveness of the EMG technique, defined as sensitivity to change, was determined by evaluating and comparing the mean log EMGAR values of COPD patients with those of the healthy subjects during T1, T2, and T3 of the diaphragm, the Int, and the left Sc. The independent t-test was used. A $P < 0.05$ was regarded as significant.

**RESULTS**

One COPD patient had a respiratory tract infection before the second test day and was excluded from the study. Furthermore, one healthy subject was excluded because of technical problems during the first measurement.

In Fig. 2, the total recording (time compressed) and a detailed recording of the averaged EMG signals and MR band signals of a representative healthy subject (Fig. 2A) and COPD patient (Fig. 2B) at T0 and during the loads (T1–T3) are presented.

At T0, the healthy subject showed low respiratory activity in the Int and the diaphragm and almost no activity in the Sc. In the COPD patient, at T0, large respiratory activity was present in all but the Abd.

During breathing against the inspiratory loads, the activity of the Int and diaphragm increased in both the COPD patient and the healthy subject. In the COPD patient, however, although the activity of the Int and the diaphragm increased at T1, it seemed to reach a plateau at T2 and T3. In the healthy subject, the activity of the Int and the diaphragm was much lower and did not reach a plateau. The activity of the Sc increased in the COPD patient at all three inspiratory loads, whereas, in the healthy subject, a small increase could be observed only at T3. In the COPD patient, a difference in the amplitude of the signal of the right and left Sc was found. This might be explained by the fact that the patient turned his head to the investigator, who stood at the left of the participant, holding the threshold device.

**Reproducibility Between Test Day 1 and Test Day 2**

The correlation coefficients for the log EMGAR values of the diaphragm, the Int, and the right and left Sc at the subsequent loads at test day 1 and test day 2 of the COPD patients and the healthy subjects are presented in Table 2.

The mean log EMGAR values against the differences between test day 1 and test day 2 of the diaphragm, the Int, and the left Sc during T1, T2, and T3 are shown in Fig. 3.

**Responsiveness**

The mean and 95% confidence interval of the log EMGAR values of the diaphragm, the Int, and the left Sc of the COPD patients compared with the healthy subjects are shown in Fig. 4.

**Diaphragm.** In the healthy subjects, the mean diaphragm activity was increased with a factor of $2.3 \pm 0.8$ at T1 (log EMGAR $= 0.36; P < 0.05$), with a factor of $2.4 \pm 0.8$ at T2 (log EMGAR $= 0.38; P < 0.05$), and with a factor of $2.7 \pm 0.7$ at T3 (log EMGAR $= 0.43; P < 0.05$), compared with baseline breathing (T0). In the COPD patients, the activity of the diaphragm increased significantly only during breathing against load T3 with a factor of $2.3 \pm 0.7$ (log EMGAR $= 0.37; P < 0.05$). At T1 and T2, the activity of the diaphragm in the COPD patients tended to increase with a factor of $1.6 \pm 0.7$ (log EMGAR $= 0.20; P = 0.07$) at both T1 and T2. However, this was not significant.

Although the activity of the diaphragm tended to increase more in the healthy subjects, no significant differences between the increases in activity in the COPD patients and healthy subjects were found.

**Int.** In the healthy subjects, the mean Int activity increased during breathing against the loads with a factor of $1.9 \pm 0.6$ ($P < 0.01$) at T1, with a factor of $2.5 \pm 0.9$ ($P < 0.01$) at T2, and with a factor of $2.9 \pm 0.9$ ($P < 0.05$) at T3, compared with T0. In the COPD patients, the activity of the Int increased with
a factor of 3.0 ± 0.6 (P < 0.01) at T1, with a factor of 3.3 ± 0.8 (P < 0.001) at T2, and with a factor of 4.3 ± 1.0 (P < 0.001) at T3, compared with T0.

Log EMGAR values of the Int were significantly higher in COPD patients compared with healthy subjects at T1 (P < 0.01). At T2 and T3, the log EMGAR values of the Int in COPD patients were not different from those of the healthy subjects.

**Left Sc.** In the healthy subjects, the mean left Sc activity increased with a factor of 1.7 ± 1.0 at T1 (P < 0.01), with a factor 1.6 ± 0.6 at T2 (P < 0.01), and with a factor of 2.5 ± 1.0 at T3 (P < 0.05), compared with T0. In the COPD patients, the mean left Sc activity increased with a factor of 3.0 ± 0.9 at T1 (P < 0.01), with a factor of 4.5 ± 0.9 at T2 (P < 0.01), and with a factor of 7.0 ± 1.1 at T3 (P < 0.01), compared with T0.

Significant differences between the COPD patients and the healthy subjects were found in the log EMGAR values of the left Sc at T2 (P < 0.01) and T3 (P < 0.05). At T1, the log EMGAR values of the COPD patients did not differ from those of the healthy subjects.

**Total inspiratory activity.** The mean and 95% confidence interval of log EMGAR values of the FD, the DD, the Int, and the left Sc of the COPD patients, compared with the healthy subjects, are shown in Fig. 5.

In the healthy subjects, the mean total inspiratory muscle activity of the healthy subjects was increased with a factor of 1.8 ± 0.6 at T1 (P < 0.01), with a factor of 2.1 ± 0.9 at T2 (P < 0.01), and with a factor of 2.6 ± 0.8 at T3 (P < 0.01), compared with T0. In the COPD patients, the mean total inspiratory muscle activity of the COPD patients was increased with a factor of 2.7 ± 0.7 at T1 (P < 0.01), with a factor of 3.4 ± 0.7 at T2 (P < 0.01), and with a factor of 4.5 ± 1.0 at T3 (P < 0.01), compared with T0.

Although there was a trend toward a higher overall activity in the COPD patients, the only significant difference between...
DISCUSSION

The present study showed that this noninvasive EMG technique has an acceptable reproducibility both in COPD patients and in healthy subjects. Moreover, this technique appeared sensitive to detect different breathing patterns in COPD patients and healthy subjects when breathing against increasing inspiratory loads.

Although this transcutaneous EMG technique could serve as a useful tool in assessing breathing patterns in healthy subjects and COPD patients, this method is still controversial. First, it has been argued that, with this technique, difficulties arise in maintaining electrode orientation with respect to the muscle fibers and in controlling for influences of variable muscle-to-electrode distance (as with variations in the amount of subcutaneous fat) (12). We minimized these influences by using the ratio of the averaged electrical muscle activity at a given instance in relation to that at baseline (EMGAR). By doing this, constant factors that influence the amount of electrical activity measured at both instances will be reduced to unity. In addition, by logarithmic transformation (log EMGAR) to zero, we corrected the actual value for the baseline value. Furthermore, we used large electrodes (diameter, 2.5 cm) for the Int and the diaphragm and placed them relatively far apart. Thus electrical activity was measured from an extensive portion of these muscles. Second, cross talk from adjacent muscles may also influence transcutaneous EMG signals (5, 24). Most sensitive to cross talk are the Sc (from the sternocleidomastoideus muscles) and the diaphragm (from the Abd). To minimize cross talk from the sternocleidomastoideus muscles, the electrodes for the Sc have to detect more specific signals. Therefore, we used relatively small bipolar electrodes for these

Fig. 3. Bland and Altman plots of the mean differences (diff) between the 2 measurements vs. the mean log EMG activity ratio (EMGAR) of the 2 measurements at day 1 and day 2 of the diaphragm (A), the intercostal muscles (B), and the left scalene muscle (C) during T1, T2, and T3. The mean differences and the 95% confidence interval (mean ± 1.96 SD) is shown for the COPD patients (dashed line) and the healthy subjects (solid line).

Fig. 4. Plots of the mean ± SD of the log EMGAR of the inspiratory muscles measured: the diaphragm (A), the intercostal muscles (B), and the left scalene muscle (C) of the COPD patients compared with the healthy subjects during T1, T2, and T3.
muscles. Cross talk from the Abd was ruled out, as almost no activity of the Abd could be detected during inspiration.

In our study, we measured the activity of both the FD and DD. As no significant differences could be found in activity patterns between the DD and FD, we considered the diaphragm as one single muscle and averaged the FD and DD signals to obtain one single diaphragm signal (3, 23).

We choose to report the left Sc signals only. We believe that tonic activity of the right sternocleidomastoideus muscle disturbed the signals obtained from the right Sc. We asked our participants to look straight ahead, but we could not prevent that they turned their heads somewhat toward the investigator. Although it has been shown that most COPD patients showed strong inspiratory contractions of the Sc and not of the sternocleidomastoideus muscle at rest (7), it cannot be excluded that, in our subjects, the activity of the sternocleidomastoideus muscle increased with inspiratory loading and disturbed the Sc.

We believe that, when more attention is given to a correct position of the head, an acceptable level of reproducibility of the signals of both Sc can be obtained with the presented EMG technique (10).

Reproducibility

A correlation of 0.8 has been reported to be acceptable for EMG measurements (11, 15). In our study, most correlations showed this degree of reproducibility. However, the method of Bland and Altman (4) may provide more appropriate information on the level of reproducibility.

As our EMG technique is only used sparsely, the limits of agreement have not been generally accepted yet. Maarsingsh et al. (15) did use the same Bland and Altman method (4) in assessing reproducibility of their data. However, in their study, the EMG data were presented as raw data and not the logarithmic relative values that we used (15). So we cannot apply their limits of agreement to our results.

It should be noticed that, for the diaphragm and for the left Sc, a systemic deviation in the mean difference was observed in both the healthy subjects and the COPD patients. This suggests that, at test day 2, there was a greater increase in the activity of these muscles compared with that at day 1. However, these differences between signal amplitude at test day 1 and test day 2 were observed during T1 only.

Furthermore, in the healthy subjects, the increased left Sc activity was caused by a large increase in log EMGAR at day 2 in only one single participant. At day 1, the left Sc activity of this subject showed serious disturbance during tidal breathing (T0), leading to unreliable and low log EMGAR values at day 1. As a consequence, a large, but artificial difference between days 1 and 2 was observed in this subject, leading to a lower correlation coefficient and a remarkable deviation in the mean difference.

The greater increase in respiratory muscle activity that the subjects showed at day 2 might be due to deterioration in their clinical condition. However, we included COPD patients who were in a clinically stable condition. Furthermore, the log EMGAR values of the diaphragm at day 2 showed the same increase in six out of seven healthy subjects, which could not be due to a clinical deterioration.

It has been shown that, during successive sessions of breathing through an inspiratory threshold, COPD patients adapt to a different breathing pattern (9). We noticed that all participants were able to handle the threshold device very soon after initiating the first load. The difference in muscle activity at T1 between test day 1 and day 2 might, therefore, be explained by the fact that both the COPD patients and the healthy subjects had to get used to the threshold during the first load at day 1. We observed that the subjects, when used to the threshold device, adopted a less shallow pattern immediately after T1. Differences in breathing patterns and depth greatly influence the pattern and the degree of recruitment of the different respiratory muscles and, consequently, the EMG signals of the individual respiratory muscles.

Responsiveness

When breathing against increasing inspiratory loads, the COPD patients used a different breathing strategy by showing significantly more increase in activity of their Sc and Int, whereas they displayed a lower increase in activity of their diaphragm, compared with healthy subjects.

Due to emphysema, the diaphragm works at an unfavorable position, causing a decreased inspiratory capacity (18, 28). Therefore, the relative contribution to force generation of the Int and accessory muscles is necessary to maintain sufficient ventilation. De Troyer et al. (7) found that COPD patients had strong inspiratory contraction of the Sc, even at rest. It seems logical that, during breathing against an inspiratory load, the contribution of the Sc increases further.

At T1, the activity of the Int increased significantly in COPD patients compared with healthy subjects. At T2 and T3, Int activity in COPD patients was still higher, but not significantly. Because the contribution of the Int to pressure generation in COPD patients is already greatly enhanced at rest, the reserves of the muscles are presumably low (28). Therefore, the increase in Int activity during incremental loading, as can be observed in the healthy subjects, is lower in COPD patients. This may explain why the differences between the log EMGAR values between the COPD patients and the healthy subjects were only significant at T1 and not at T2 and T3.

We averaged the signals of the FD, DD, Int, and the left Sc to determine whether the EMG technique was a sensitive method to measure changes in overall inspiratory muscle activity. The increase in overall inspiratory muscle activity tended to be higher in the COPD patients than in the healthy subjects at all three loads, with a significantly higher increase.
in the COPD patients at T1. We found a linear relationship between mean log EMGAR and load, which means that the mean averaged activity ratio of the muscles that we measured was exponentially related to the inspiratory load.

In conclusion, the EMG technique was shown to be reproducible and sensitive to assess changes in respiratory muscle activity and breathing patterns in healthy subjects and in patients with COPD. This technique can be used to assess the activity of the different respiratory muscles simultaneously, both at rest and during inspiratory loading. Its noninvasive and nonintrusive character makes this technique useful in assessing respiratory activity and breathing patterns during different intervention programs.

ACKNOWLEDGMENTS

We are grateful to D. J. van Hoogstraten for editorial advice.

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