

## Neuromuscular electrostimulation as an adjuvant therapy to pulmonary rehabilitation programs in chronic obstructive pulmonary disease

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### Abstract

**Introduction.** Chronic obstructive pulmonary disease (COPD) is commonly associated with a vicious circle of sedentary lifestyle - deconditioning - muscular dysfunction. High-frequency neuromuscular electrostimulation has demonstrated beneficial effects among subjects with muscle weakness. This study aimed to evaluate the benefits of merging pulmonary rehabilitation program (PRP) with neuromuscular electrostimulation in patients with very severe COPD. **Material and methods.** The study included 38 males with clinically stable COPD, who were divided in 2 groups: group A-19 patients that underwent a PRP of 5 sessions/week for 4 weeks and group B-19 patients that underwent intercostal and lower extremity muscle electrostimulation (5 sessions/week for 4 weeks, 60 min /session) in association with the same type of PRP. Saint Georges’s Respiratory Questionnaire (SGRQ), Modified Medical Research Council (mMRC) dyspnea scale, spirometry, maximal inspiratory pressure (P<sub>I</sub>max) and maximal expiratory pressure (P<sub>E</sub>max), six minutes walking test (6MWT) and bio-electrical impedance were examined before and after the intervention. **Results.** Electrostimulation applied in group B increased muscle mass ( $50.15 \pm 0.61\text{kg}$  vs  $53.97 \pm 0.87\text{kg}$ ,  $p < 0.001$ ), P<sub>E</sub>max ( $5.41 \pm 0.25$  vs post  $6.79 \pm 0.22$ ,  $p < 0.0003$ ) and improved mMRC score ( $2.68 \pm 0.15$  vs  $2.10 \pm 0.15$ ,  $p < 0.0109$ ), 6MWT ( $369.6 \pm 10.77\text{m}$  vs post:  $445.6 \pm 6.03\text{m}$ ) and SGRQ ( $61.32 \pm 1.83$  vs.  $44.95 \pm 1.94$ ,  $p < 0.0001$ ). In group B only SGRQ score ( $55.05 \pm 1.32$  vs.  $50.05 \pm 1.51$ ,  $p = 0.018$ ) was improved after PRP. **Conclusion.** A protocol which combines PRP with neuromuscular electrical stimulation in patients with very severe forms of COPD, has greater beneficial effect on dyspnoea, exercise tolerance, muscle mass toning and quality of life, compared with PRP alone.

**Key words:** COPD, muscular dysfunction, neuromuscular electrostimulation, pulmonary rehabilitation program,

### Introduction

In the last century, due to medical innovations, we are facing a decrease in the morbidity and mortality caused by respiratory infections like pneumonia or tuberculosis and a rise in life expectancy (1). On the other hand, in developed countries this phenomenon has led to an increased prevalence of age-related chronic respiratory diseases (2-3): COPD, asthma, emphysema, lung cancer, obstructive sleep apnoea, idiopathic pulmonary fibrosis etc. which represent a significant burden for the health care services (4-10). COPD is a disorder characterized by chronic incomplete reversible airway limitation (11-12). During the chronic evolution of this disease, patients develop dyspnoea, fatigue, limited exercise capacity, symptoms that will lead to a vicious circle of sedentary lifestyle - deconditioning - muscular dysfunction (13,14) Muscle weakness is independent of airflow obstruction severity of and is a significant risk factor for falls in this population (15-16).

International guidelines recommend that patients with COPD should be included in PRP, in order to slow down the respiratory decline and to prevent muscle loss (11,12). These programs have been designed to optimize physical function, social performance and autonomy of patients with chronic respiratory diseases.

High-frequency neuromuscular electrostimulation has demonstrated beneficial effects among subjects with muscle weakness, especially in quadriceps muscle (17). It can be used alone or in association with other rehabilitation techniques.

### Study aim

The objective of this study was to investigate if the association of neuromuscular electrostimulation to a pulmonary rehabilitation program will have greater benefits on muscle toning and exercise tolerance, then PRP alone, in patients with very severe COPD.

## Materials and methods. Study design

Before participating in the study, patients signed an informed consent form. The ethical board of the “Victor Babes” Hospital for Infectious and Lung Diseases, Timisoara, Romania approved the study.

Thirty-eight males with clinically stable COPD participated in this prospective study. All subjects were diagnosed with very severe COPD according to GOLD/ATS criteria. The inclusion criteria were age of 40–75 years, eligibility to participate in exercise training, no acute exacerbations within the 3 month and no change in respiratory medication within the past 4 weeks. Exclusion criteria: orthopedic impairment, neuromuscular disorders, recent stroke or heart attack, advanced heart failure, aortic stenosis or pulmonary artery pressure >50 mmHg.

Subjects were divided in two study groups: Group A included 19 patients that underwent a PRP of 5 sessions/week for 4 weeks and Group B included 19 patients that underwent intercostal and lower extremity muscle electrostimulation (5 sessions/week for 4 weeks, 60 min per session) in association with the same type of PRP.

The PRP consisted in stretching exercises and endurance training: 60 min of treadmill and stationary bicycle, at 80% of each patient’s maximal heart rate. The PRP also included quadriceps resistance training and breathing exercises. The neuromuscular electrostimulation was performed using a Cefar Activ device. A prefigured software which combined aerobic exercises, strength exercises and body toning for the quadriceps and for intercostal muscles, was used. The procedure consisted in applying the electrodes to proximal and distal endpoints of quadriceps and intercostal muscle body. A commutative, symmetric current of 20-35 Hz frequency and 15-90 mA intensity, was used for 60 minutes per day, 5 days/week. The intensity was enlarged until a strong muscle contraction was visible or to the maximum toleration level.

At the beginning of the study, all subjects demographic information, smoking and medical history, physical examination were recorded. They completed SGRQ questionnaire, performed spirometry (Vitalograph ALPHA), P<sub>Imax</sub> and P<sub>E<sub>max</sub></sub>, 6MWT test. The body composition was analysed via bioimpedance (BFAT Model IOI 353). The body mass index (BMI), muscle mass (kg) and fat-free mass (%) were recorded. Dyspnoea was evaluated using the mMRC dyspnoea scale. The same investigations were performed at the end of the 3 weeks PRP.

The SGRQ as used to assess the health-related quality of life. The SGRQ includes 50 items. Total score is ranging from 0 to 100. A zero score indicates no impairment of health-related quality of life (18).

Respiratory muscle strength can be evaluated by measuring P<sub>Imax</sub> and P<sub>E<sub>max</sub></sub>. The P<sub>Imax</sub> correlates with the diaphragm and other inspiratory muscles strength, while P<sub>E<sub>max</sub></sub> correlates with abdominal muscles and expiratory muscles strength.

The 6MWT is used to assess aerobic capacity and endurance. The distance covered in 6 minutes reflects the changes in performance capacity after a pulmonary rehabilitation program.

## Statistical analysis

Data were collected using GraphPad Prism 7. The results are presented as mean ± standard deviation for continuous variables with Gaussian distribution, median (interquartile range) for continuous variables without Gaussian distribution, and percentage for categorical variables. A P value of <0.05 was considered statistically significant.

## Results

The baseline characteristics of the studied groups are listed in table 1. Subjects from group B were older than those from group A (Table 2,3).

No statistically significant differences were noted in the spirometric values between the studied groups both pre- and post-intervention.

	<b>Group A</b>	<b>Group B</b>	<b>P</b>
<b>Age</b>	57.53 ± 1.49	63.11 ± 1.72	0.019*
<b>FVC (L)</b>	2.46 ± 0.14	2.22 ± 0.12	0.221
<b>FVC (%)</b>	62.05 ± 3.34	60.05 ± 3.55	0.684
<b>FEV1 (L)</b>	1.02 ± 0.06	0.92 ± 0.05	0.260
<b>FEV1 (%)</b>	32.89 ± 2.51	32.11 ± 2.39	0.821
<b>FEV1/FVC</b>	44.89 ± 3.26	46.26 ± 2.77	0.751
<b>BMI</b>	27.21 ± 0.69	27.42 ± 1.07	0.870

In group B, P<sub>E<sub>max</sub></sub> has significantly increased after the program (P<sub>E<sub>max</sub></sub> pre 5.41 ± 0.25 vs post 6.79 ± 0.22, p<0.0003). There was no significant effect of pulmonary rehab or pulmonary rehab combined with electrostimulation on P<sub>Imax</sub>. (Table 3).

	<b>PRE (Mean ± SEM)</b>	<b>POST (Mean ± SEM)</b>	<b>P</b>
<b>PIMAX</b>	7.12 ± 0.34	7.35 ± 0.33	0.647
<b>PEMAX</b>	5.66 ± 0.16	5.78 ± 0.41	0.774
<b>mMRC</b>	2.26 ± 0.12	2.10 ± 0.16	0.463
<b>MM</b>	51.21 ± 0.89	51.65 ± 0.99	0.742
<b>FFM</b>	33.16 ± 0.88	34.18 ± 0.73	0.382
<b>6MWD</b>	359.8 ± 15.6	381.6 ± 16.43	0.345
<b>SGRQ</b>	55.05 ± 1.32	50.05 ± 1.51	0.018*

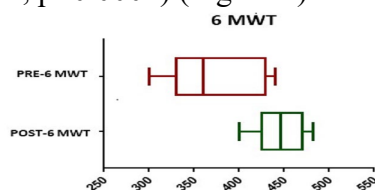
Group B registered a decreased dyspnoea after the intervention (mMRC pre  $2.68 \pm 0.15$  vs mMRC post  $2.10 \pm 0.15$ ,  $p < 0.0109$ ) (Table 3) while in group A showed no statistically significant improvement.

**Table 3. Pre-intervention and post-intervention characteristics for Group B**

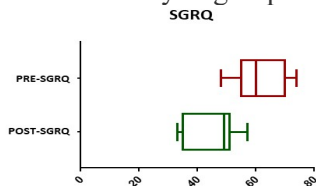
	PRE (Mean $\pm$ SEM)	POST (Mean $\pm$ SEM)	P
PIMAX	$7.09 \pm 0.29$	$7.89 \pm 0.34$	0.0891
PEMAX	$5.41 \pm 0.25$	$6.79 \pm 0.22$	0.0003*
mMRC	$2.68 \pm 0.15$	$2.10 \pm 0.15$	0.0109*
MM	$50.15 \pm 0.61$	$53.97 \pm 0.87$	0.001*
FFM	$33.04 \pm 0.65$	$34.41 \pm 0.92$	0.241
6MWD	$369.6 \pm 10.77$	$445.6 \pm 6.03$	$< 0.0001^*$
SGRQ	$61.32 \pm 1.83$	$44.95 \pm 1.94$	$< 0.0001^*$

The body composition changed in the electrostimulation group (Table 3). Muscle mass (MM) increased only in group B (pre:  $50.15 \pm 0.61$  kg vs post:  $53.97 \pm 0.87$  kg,  $p < 0.001$ ) while in group A (pre:  $51.21 \pm 0.89$  kg vs post  $51.65 \pm 0.99$  kg,  $p = 0.742$ ) no significant improvements were noticed.

Pre-rehabilitation, the 6MWT results did not differ significantly between the studied groups. Post-rehabilitation, a significant increase of distance walked in the 6MWT was observed only in group B (pre:  $369.6 \pm 10.77$  m vs post:  $445.6 \pm 6.03$  m) (Figure 1). The increase in the distance walked was 76 m for group B and only 21.8 m for group A. Patients from both groups reported an improvement of health-related quality of life (group A, SGRQ pre  $55.05 \pm 1.32$  vs. SGRQ post  $50.05 \pm 1.51$ ,  $p = 0.018$  and group B SGRQ pre  $61.32 \pm 1.83$  vs. SGRQ post  $44.95 \pm 1.94$ ,  $p < 0.0001$ ) (Figure 2)



**Fig.1.** Pre-rehabilitation, the 6MWT results did not differ significantly between the studied groups. Post-rehabilitation, a significant increase of distance walked in the 6MWT was observed only in group B



**Fig.2.** Patients from both groups reported an improvement of health-related quality of life (group A, SGRQ pre  $55.05 \pm 1.32$  vs. SGRQ post  $50.05 \pm 1.51$ ,  $p = 0.018$  and group B SGRQ pre  $61.32 \pm 1.83$  vs. SGRQ post  $44.95 \pm 1.94$ ,  $p < 0.0001$ )

## Discussion

The present study showed that association of neuromuscular electrostimulation to a PRP, will have greater benefits on muscle toning, exercise tolerance and quality of life, then pulmonary rehabilitation program alone, in patients with very severe COPD.

Subjects from the electrostimulation group were older then those from standard pulmonary rehabilitation group. This observation correlated with better results in this group, emphasizes the benefits of electrostimulation.

We used electrostimulation on the intercostal muscles but no significant differences in the spirometric values between the studied groups both pre- and post-intervention, were noticed. This observation is supported also by other authors (19). However, Vieira et al. assessed the effect of electrostimulation on the dynamic hyperinflation after 8 weeks of therapy. The neuromuscular stimulation increased FEV1, FEV1/FVC, 6MWT and reduced SGRQ ( $P < 0.01$ ) (20). Lau et al., using a different protocol on the stellate ganglion region, have demonstrated a significant increase in FEV1 post electrostimulation program (21). Thus, we can assume that a longer period of therapy and a different thoracic stimulation region, could be the keys for an effective respiratory function rehabilitation.

We observed an increased expiratory muscle strength after the electrostimulation, but the inspiratory muscle strength change did not reach the statistical significance cut off. This observation is supported also by other papers (20). We can assume that a longer period of therapy could be more efficient on respiratory muscle strength.

The muscle mass has increased in the electrostimulation group, but no modification was recorded in the pulmonary rehabilitation group. Dal Corso et al. did not find significant changes in muscle mass, but an increase in type II muscle fibres and a decrease in type I (22).

A significant difference in the 6 MWT test was observed in the electrostimulation group. According to ATS/ERS guidelines a 47 m improvement in the 6MWT after an PRP intervention is a clinically significant (23). We observed an increase of 76 m after electrostimulation and only 21.8 m in the standard rehabilitation program. We have to keep in mind that these results are obtained in cohorts who included only severely deconditioned patients with COPD, GOLD 4.

It is important for clinicians to assess the health related quality of life among COPD patients, as this is a good indicator of disease severity (24). Among many specific instruments available in literature, SGRQ reflects the most complex image of diseases impact on patients daily life. In the current study, patients from both groups reported an improvement of health related quality of life (group A, SGRQ pre  $55.05 \pm 1.32$  vs. SGRQ post  $50.05 \pm 1.51$ ,  $p=0.018$  and group B SGRQ pre  $61.32 \pm 1.83$  vs. SGRQ post  $44.95 \pm 1.94$ ,  $p<0.0001$ ) observation also supported by other authors (20).

The disparities between the results obtained in different studies available in literature, can be explained by distinct electrostimulation and pulmonary rehabilitation protocols. A difference in the intensity and duration of muscular stimulation can highly influence the outcome of the intervention (25-26). Studies who used electrostimulation with higher intensities (15-90 mA) and lower frequencies (5-35 Hz) showed an increase in muscle mass (27-28) whereas other studies (22,29) who used lower intensities (10-45 mA) and higher frequencies (50 Hz) found no changes in muscle mass.

Future research on electrostimulation, should also address other pathologies who associate dyspnoea and muscle dysfunction, due to the high prevalence of age-related chronic respiratory diseases.

**Limitations.** The first limitation of this research was the short period of observation due to the fact that Romanian National Health System provides financial support only for a three-week pulmonary rehabilitation programme. In contrast, other studies lasted around 4 to 8 weeks. Secondly, the small sample size did not allow us to analyse sub-groups which could clarify some of the clinical changes. Further studies are needed to analyse the effects of merging neuromuscular stimulation with pulmonary rehabilitation programs in COPD patients and to evaluate the impact on hospitalizations rate and survival.

**Conclusion.** A protocol which combines pulmonary rehabilitation with neuromuscular electrical stimulation of the intercostal and lower limbs muscles, in patients with very severe forms of COPD, has grater beneficial effect on dyspnoea, exercise tolerance, muscle mass toning and quality of life, compared with pulmonary rehabilitation alone.

#### **Declaration of conflict of interests**

The authors declare that there is no conflict of interest regarding the publication of this article.

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