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KLİNİK ÇALIŞMA
RESEARCH ARTICLE

Comparison of the effects of neuromuscular electrical stimulation and endurance training in patients with severe chronic obstructive pulmonary disease

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SUMMARY

Comparison of the effects of neuromuscular electrical stimulation and endurance training in patients with severe chronic obstructive pulmonary disease

Introduction: *In severely disabled patients who are not capable of following formal pulmonary rehabilitation (PR) and/or tolerating higher training intensities, neuromuscular electrical stimulation (NMES) has been successfully utilized as a localized training method.*

Materials and Methods: *In this non-randomized controlled observational study 50 patients with severe chronic obstructive pulmonary disease (COPD), who were allocated into two groups. Endurance training group (ET) (n= 27) and NMES group (n= 23). To compare the effects of NMES and ET on health-related quality of life (HRQOL), exercise capacity, muscle strength, dyspnea, psychological status, and body composition in patients with severe COPD. Before and after PR program, the study parameters were assessed using the Medical Research Council (MRC) scale, incremental and endurance shuttle walking tests (ISWT, ESWT), manual muscle testing (MMT), the St. George's Respiratory Questionnaire (SGRQ), bioelectrical impedance analysis, and the Hospital Anxiety and Depression Scale (HADS).*

Results: *After the PR program, walking distance and endurance time significantly increased in both groups (p< 0.001 for each), whereas the MRC scores of both groups significantly decreased (p< 0.001 for each). In the ET group, significant decreases were noted in all domains of SGRQ and HADS. In the NMES group, significant improvements were observed in the HADS scores and in all SGRQ domain except symptom domain. No significant differences were observed between the NMES and ET groups regarding the changes from baseline to after PR program in walking dis-*

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tance (p= 0.140), endurance time (p= 0.376), the MRC (p= 0.540), HRQOL (p> 0.05) and HADS (p> 0.05) scores, body-mass index (BMI) (p= 0.49), fat-free mass (FFM) (p= 0.50) and fat-free mass index (FFMI) (p= 0.94).

Conclusion: *NMES can be used as an effective treatment strategy in PR programs for peripheral muscle training in patients with severe COPD.*

Key words: *COPD, dyspnea, pulmonary rehabilitation*

ÖZET

Ciddi kronik obstrüktif akciğer hastalığı olan olgularda nöromusküler elektriksel stimülasyonu ve endurans eğitim etkinliğinin karşılaştırılması

Giriş: *Ciddi hastalık ve kas disfonksiyonu nedeniyle egzersiz eğitimine aktif katılamayan KOAH'lı olgularda periferik kasların elektriksel stimülasyonu bir tedavi stratejisi olarak pulmoner rehabilitasyon (PR) programlarında başarıyla kullanılabilecek metodtur.*

Materyal ve Metod: *Nonrandomize kontrollü gözlemsel çalışmaya ileri evre KOAH'ı olan 50 olgu alındı. Olguların 27'sine endurans eğitimi, 23'üne ise nöromusküler elektriksel stimülasyon (NMES) uygulanmak üzere iki gruba ayrıldılar. PR programı öncesi ve sonrasında olguların nefes darlığı MRC ile, egzersiz kapasitesi artan hızda mekik yürüme testi (AHMYT) ile, periferik kas gücü manuel kas testi ile yaşam kalitesi SGRQ anketi ile, psikolojik durumları HAD skalası ile vücut kompozisyonu ise bioelektriksel impedans yöntemi ile değerlendirildi.*

Bulgular: *Her iki grupta da pulmoner rehabilitasyon programı sonrası MRC'de azalma (p< 0.001) AHMYT mesafesi ve endurans süresinde artış (p< 0.001) saptanırken, endurans eğitimi uygulanan grupta SGRQ anketinin tüm alt başlıklarında ve HAD skorlarında azalma, NMES uygulanan grupta ise SGRQ anketinin semptom skoru hariç diğer tüm alt başlıklarında ve total skorunda, HAD skorlarında iyileşme saptandı. PR programı sonrası NMES ve endurans eğitim etkinlikleri arasında tüm parametrelerdeki kazanımların benzer düzeylerde olduğu görüldü.*

Sonuç: *İleri evre KOAH'da nöromusküler elektriksel stimülasyon PR programlarında periferik kas eğitiminde kullanılabilecek etkin bir yaklaşımdır.*

Anahtar kelimeler: *KOAH, dispne, pulmoner rehabilitasyon*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) results in a progressive worsening in lung function, dyspnea, health-related quality of life (HRQOL), and exercise capacity (1-4). In COPD patients, peripheral and respiratory muscle dysfunction have been suggested as the primary determinants of decreased exercise capacity. Skeletal muscle dysfunction is associated with malfunctioning of the muscle and net loss of muscle mass (5). Weight loss, which is observed in the majority of patients with COPD, leads to peripheral muscle dysfunction and weakness (6). Reasons of changes in skeletal muscle include sedentary lifestyle, systemic inflammation, hypoxia, hypercapnia, oxidative stress, medications (systemic corticosteroids, etc.), myopathy, nutritional depletion, anabolic hormone levels, abnormal protein turnover, mitochondrial abnormalities, and muscle disuse (5, 7, 8). Strength, endurance, and fatigability of the peripheral muscle are impaired in patients with COPD (5).

It has been well established that pulmonary rehabilitation (PR) enhances standard therapy to relieve symptoms and optimize function independent of the disease stage (9, 10). Improvement in exercise tolerance of COPD patients has been demonstrated with exercise training, typically as a component of PR. However, physical training could be especially difficult in patients with intense breathlessness at rest or on minimum exertion. In severely disabled patients who are not capable of following formal PR and/or tolerating higher training intensities, neuromuscular electrical stimulation (NMES) has been successfully utilized as a localized training method (11).

The present study aimed to compare the effects of NMES and endurance training on HRQOL, exercise capacity, muscle strength, dyspnea, and psychological status and body composition in patients with severe COPD.

MATERIALS and METHODS

In this non-randomized controlled observational study 50 patients with severe COPD who were admitted to the Pulmonary Rehabilitation Outpatient Clinic of Atatürk Chest Disease and Chest Surgery Training and Research Hospital. A written informed consent was obtained from each patient before all procedures. The study was approved by the Ethical Committee of Atatürk Chest Disease and Chest Surgery Training and Research Hospital.

Inclusion criteria were clinical diagnosis of COPD according to the Global Initiative for Obstructive

Lung Disease (GOLD) criteria (9), clinical stability (no exacerbation over the previous 30 days), and no prior participation in a PR program. Patients with comorbidities such as heart, orthopedic, or neurologic diseases were excluded from the study.

The patients were allocated into two groups: those who performed endurance training (ET group, n= 27) and those who received NMES (NMES group, n= 23). Because patients had severe dyspnea, they did not tolerate ET. These patients were included NMES group. Before and after PR program, the following measures were used for all patients:

1. Medical Research Council (MRC) scale for the assessment of dyspnea sensation during activities of daily living (12),
2. Incremental and endurance shuttle walking tests (ISWT and ESWT) for the evaluation of exercise capacity (13,14),
3. Manual muscle testing (MMT) for the measurement of peripheral muscle strength (15),
4. SGRQ (16),
5. The bioelectrical impedance analysis (BIA) for the estimation of body composition (17),
6. HADS for the assessment of psychological status (18).

Depending on the baseline findings, each patient underwent a comprehensive, patient-specific, outpatient-based, and directly supervised PR program. The PR program included educational support, exercise training, psychological counseling, and a nutritional intervention, if needed. Educational support covered disease education and education of families, bronchial hygiene and breathing control techniques, energy conservation, and relaxation. Educational sessions were delivered by two chest physicians, two physical therapists, a dietician, two respiratory nurses, and a psychologist.

Aerobic exercises and active strengthening exercises for upper and lower extremities were performed in the ET group. The exercise program was prescribed 3 days a week for 8 weeks (2 days in hospital under direct supervision and 1 day at home without supervision). Exercise workloads were: walking on the treadmill for 15 min at the peak oxygen consumption (VO2) of 60%-85% and cycling for 15 min on a stationary bicycle at a peak Watt of 50%-75%; 30 min in total.

In 23 patients who were allocated to NMES group, NMES with active strengthening exercises were performed on specific muscle groups (quadriceps and deltoid muscle) in the upper and lower extremities for 10 weeks (2 days a week at hospital under direct supervision). NMES was performed using a symmetrical biphasic waveform at 300-400 msec of current duration and with a 50 Hz frequency for 15 min. The intensity of the current was increased up to the patients' maximum tolerance at which contraction was achieved. No side effects (such as skin lesions or muscle pain) related to NMES application were observed. The NMES treatment was well tolerated by the participants.

At the end of the PR program, effectiveness of the endurance training and NMES were compared. Study design was shown in Figure 1.

Statistical Analysis

Data analyses were performed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 11.5. All data were expressed as mean ± standard deviation. The Mann-Whitney U test was used for inter-group comparisons according to change in the study parameters from baseline to after PR program. The Wilcoxon test was used for intra-group comparisons of parameters at baseline and after PR program. p value of <0.05 was considered statistically significant.

RESULTS

The mean age, the mean pack year smoking history, and the mean percent predicted forced expiratory volume in 1 second (FEV_1) value of the patients in the ET group (n= 27) were 62.81 ± 7.18 years, 45.98 ± 24.24, and 27.33 ± 8.20, respectively. The mean age,

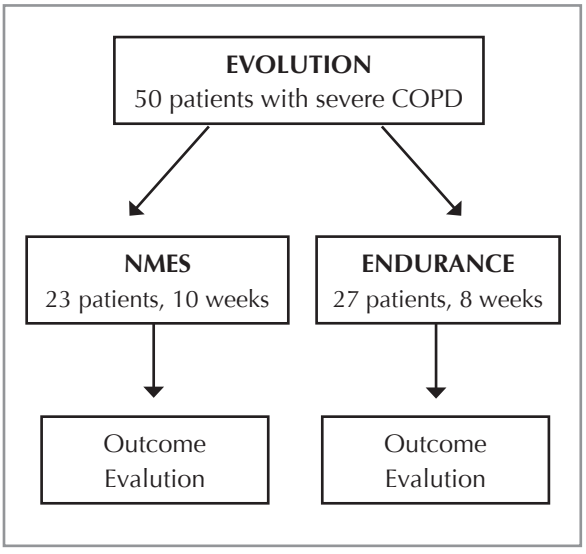

Figure 1. Study design.

the mean pack year smoking history, and the mean percent predicted FEV_1 value of the patients in the NMES group (n= 23) were 63.25 ± 10.10 years, 42.26 ± 30.83, and 25.91 ± 7.26, respectively. No significant differences were observed between the two groups in terms of age, pack year smoking history, and FEV_1 value (p> 0.05 for each; Table 1).

Exercise Capacity

After the PR program, significant increases both in walking distance and endurance time were observed in the NMES group (56.95 ± 37.68 m, p< 0.001), (4.55 ± 6.56 min, p< 0.001), and in the ET group (80.18 ± 57.75 m, p< 0.001), (5.77 ± 6.16 min: p< 0.001) respectively. There were no significant differences between the NMES and ET groups with respect to the changes from baseline to after PR program in walking distance and endurance time (p= 0.140, p= 0.376) (Table 2).

Dyspnea Sensation

After the PR program, a significant decrease in the MRC score was observed both in the NMES and ET groups (p< 0.001 and p< 0.001, respectively). There was no significant difference between the two groups with respect to the changes from baseline to after PR program in the MRC score (p= 0.540) (Table 2).

Muscle Parameters

There were significant increases in the muscle strengths of upper and lower extremities evaluated with MMT (Table 3); however, the level of gains were similar in the groups (p> 0.05) (Table 2).

Health Related Quality of Life and Psychological Status

In the ET group, a significant decrease was observed in the score of all domains of the SGRQ and HADS after the PR program. In the NMES group, significant

Table 1. Demographic and clinical characteristics of the study groups

Characteristics	NMES group (n= 23)	ET group (n= 27)	p
Age (years)	63.25 ± 10.10	62.81 ± 7.18	> 0.05
Pack year smoking history	42.26 ± 30.83	45.98 ± 24.24	0.89
FEV_1, % predicted	25.91 ± 7.26	27.33 ± 8.20	0.52
FEV_1/FVC ratio, %	51.08 ± 14.20	39.85 ± 6.84	< 0.001

FEV_1: Forced expiratory volume in 1 second; FVC: Forced vital capacity. Data are presented as mean ± standard deviation.

Table 2. Comparison of the gainings between the groups

	NMES group (n= 23)	ET group (n= 27)	p
MRC	-1.08 ± 0.84	-1.25 ± 0.76	0.540
ISWT (m)	56.95 ± 37.68	80.18 ± 57.75	0.140
ESWT (min)	4.55 ± 6.56	5.77 ± 6.16	0.376
SGRQ symptom	-5.5 ± 18.6	-14.3 ± 19.72	0.06
SGRQ-activity	-16.2 ± 20.45	-19.5 ± 21.56	0.59
SGRQ-impact	-23.50 ± 26.44	-22.9 ± 23.54	0.88
SGRQ total	-18.2 ± 19.97	-20.4 ± 17.06	0.68
HADS anxiety	-1.82 ± 3.15	-2.3 ± 3.0	0.29
HADS depression	-2.17 ± 2.9	- 1.9 ± 3.0	0.95
BMI, kg/m^2	0.31 ± 1.41	0.16 ± 0.98	0.49
FFMI, kg/m^2	0.14 ± 1.01	0.06 ± 0.71	0.94
Deltoid			
Right	0.56 ± 0.50	0.37 ± 0.56	0.14
Left	0.47 ± 0.51	0.25 ± 0.52	0.08
Quadrices			
Right	0.34 ± 0.57	0.48 ± 0.50	0.43
Left	0.39 ± 0.58	0.48 ± 0.50	0.63

Table 3. Outcomes at baseline and after the PR program

	NMES group (n= 23)			ET group (n= 27)		
	Baseline	**After PR**	**p**	**Baseline**	**After PR**	**p**
MRC	4.3 ± 0.9	3.2 ± 1.0	**< 0.001**	3.8 ± 0.8	2.5 ± 0.7	**< 0.001**
ISWT (m)	90.6 ± 87.7	147.6 ± 90.0	**< 0.001**	158.3 ± 88.6	238.5 ± 108.6	**< 0.001**
ESWT (min)	3.0 ± 5.5	7.6 ± 6.5	**< 0.001**	4.5 ± 5.2	10.3 ± 6.3	**< 0.001**
SGRQ-symptom	69.0 ± 14.8	63.4 ± 14.5	0.167	64.9 ± 17.8	50.6 ± 18.3	**< 0.001**
SGRQ-activity	87.5 ± 15.9	71.2 ± 21.2	**< 0.001**	78.0 ± 20.4	58.5 ± 22.2	**< 0.001**
SGRQ-impact	58.9 ± 20.7	35.4 ± 20.4	**< 0.001**	47.8 ± 23.0	25.0 ± 17.5	**< 0.001**
SGRQ total	69.4 ± 16.2	51.2 ± 16.8	**< 0.001**	60.0 ± 18.7	39.6 ± 16.1	**< 0.001**
HADS anxiety	9.4 ± 3.4	7.6 ± 2.8	**< 0.05**	8.7 ± 3.2	6.3 ± 2.6	**< 0.001**
HADS depression	10.1 ± 2.5	7.9 ± 3.6	**< 0.01**	8.8 ± 2.5	6.8 ± 2.8	**< 0.01**
BMI, kg/m^2	21.9 ± 5.8	22.2 ± 5.5	0.293	22.4 ± 4.2	22.6 ± 3.9	0.386
FFM, kg	44.4 ± 6.2	45.2 ± 7.1	0.164	49.5 ± 6.3	49.7 ± 6.2	0.401
FFMI, kg/m^2	17.0 ± 1.9	17.1 ± 2.1	0.506	17.9 ± 1.9	18.0 ± 1.8	0.632
Deltoid						
Right	3.86 ± 0.75	4.43 ± 0.58	< 0.01	4.44 ± 0.75	4.81 ± 0.39	< 0.01
Left	3.82 ± 0.77	4.30 ± 0.40	< 0.05	3.82 ± 0.77	4.70 ± 0.54	< 0.05
Quadrices						
Right	4.04 ± 0.82	4.39 ± 0.72	< 0.05	4.33 ± 0.6	4.39 ± 0.72	< 0.001
Left	4.04 ± 0.82	4.43 ± 0.72	< 0.001	4.33 ± 0.6	4.81 ± 0.48	< 0.001

MRC: Medical Research Council, ISWT: Incremental shuttle walking test, ESWT: Endurance shuttle walking tests,
SGRQ: the St. George's Respiratory Questionnaire; BMI: Body mass index, FFM: Fat-free mass; FFMI: Fat-free mass index.

improvements were observed in the impact, activity and total domains of the SGRQ and in the HADS score after the PR program, whereas no significant improvement was noted in the symptom domain score of the SGRQ (p= 0.167). No significant differences was noted between the two groups with respect to the changes from baseline to after PR program in the HRQOL (p= 0.06 for symptom domain, p= 0.59 for activity domain, p= 0.88 for impact domain, and p= 0.68 for total domain) and HADS scores (p= 0.29 for anxiety domain and p= 0.95 for depression domain) (Table 2).

Nutritional Status

Baseline fat-free mass (FFM) value of the NMES group was significantly lower than that of the ET group (p< 0.01). After the PR program, no significant change was observed in the BMI, FFM and FFMI values of the two groups (p> 0.05). Moreover, there were no significant differences between the two groups with respect to the changes in the BMI, FFM and FFMI values from baseline to after PR program (p= 0.49, p= 0.50, and p= 0.94, respectively) (Table 2).

DISCUSSION

Exercise training, which is performed to improve the exercise tolerance and to increase functional capacity in COPD patients, is the most important component of the PR programs (19-21). It is known that exercise intensity is of importance in achieving physiological gains of exercise, and high-intensity exercise training produce a greater physiological response and a greater improvement in submaximal exercise tolerance as compared to low-intensity exercise training. In their study, Casaburi et al. compared physiological responses in patients with COPD in whom high- and low-intensity exercise protocols were performed; they observed reductions in the lactate level, ventilation, oxygen consumption and heart rate in the high-intensity exercise group after PR program and reported that the high-intensity exercise resulted in greater physiological gains after PR program (22). However, these results do not indicate that all patients with COPD may tolerate high-intensity exercises. Passive training of specific muscle groups with the use of NMES is used as a novel treatment strategy in patients with advanced stage COPD who are unable to participate in active exercise due to severe ventilatory limitation and dyspnea. In the

study by Zanotti et al., a significant improvement in the muscle strength and a decrease in the number of days needed to transfer from bed to chair were achieved with the use of NMES in addition to classical active limb mobilization in bed-bound COPD patients receiving mechanical ventilation, with marked peripheral muscle hypotonia and atrophy (23). In the present study, the effects of NMES and endurance training were compared in dyspneic patients with severe COPD, and similar physiological gains were observed.

In another study conducted on NMES, which specifically evaluated the effect of transcutaneous electrical stimulation in frail patients assigned to an inpatient rehabilitation program after an acute exacerbation, and it was shown that the addition of NMES to regular exercise training led to an increase in isometric quadriceps muscle strength (p= 0.03) (24). In their study, Bourjeily-Habr et al. reported a significant improvement in isokinetic leg extension peak torque (+39%) in patients with COPD (FEV_1, 38% predicted) after a 6-week electrostimulation training period as compared with the sham-treated group (25). The results of the present study were in accordance with those of the above-mentioned randomized controlled studies reporting significant increases in peripheral muscle strength in stable COPD patients. In the study by Dal Corso et al., the small changes on the amount of contractile protein were reported to be largely restricted to type II fibers in a group of patients with moderately impaired COPD after a 6-week of NMES training; however, this was not translated into increased skeletal muscle strength and exercise capacity (26). The present study also supported the use of NMES in individuals with severe disability.

In the present study, although not significant, baseline MRC score of the patients in the NMES group were higher than that of the patients in the ET group. However, using a 10-week NMES training program, functional capacity of the patients could be enhanced, which was indicated by an improvement in dyspnea sensation during activities of daily living. Based on these findings, NMES can be suggested to be a safe and effective strategy in the rehabilitation of severe COPD patients with incapacitating breathlessness. As compared with conventional exercise training, the virtual absence of ventilatory stress during passive exercise, indicating the smaller muscle mass involved, is the primary advantage of NMES in patients with COPD. Neder et al. performed quadriceps femoris NMES training program in 15 patients with advanced COPD (27). They concluded that the use of short-term electrical stimulation in selected lower limb muscles involved in ambulation could result in an improvement in muscle strength and endurance, whole body exercise tolerance, and breathlessness during daily activities.

In conclusion, NMES can be used as an effective treatment strategy in PR programs for peripheral muscle training in patients with severe COPD.

CONFLICT of INTEREST

None declared.

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