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REVIEW PAPER

Effects of Neuromuscular Electrical Stimulation on Peripheral Muscle Strength and Exercise Tolerance in Chronic Obstructive Pulmonary Disease Patients: A Systematic Review

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Abstract

Currently, Chronic Obstructive Pulmonary Disease (COPD) is perceived not only as a pulmonary disease, but more as a systemic disease affecting the functioning of other organs including the locomotor system. The application of physical therapy in patients with COPD has been found to be safe and beneficial. Neuromuscular Electrical Stimulation (NMES) treatment is particularly beneficial for patients who are unable or unwilling to participate in daily activities or regular physical exercise. The efficacy of this technique has not yet been fully demonstrated in patients with COPD. Therefore, this study aimed to evaluate the effects of NMES on peripheral muscle strength and exercise tolerance in COPD patients. As part of the literature review for this study, seven studies over the last 19 years have been taken into consideration. The review included the following databases: Physiotherapy Evidence Database (PEDro), Google Scholar, and PubMed. Based on our literature review, we concluded that NMES has positive effects on increasing peripheral muscle strength and exercise tolerance in COPD patients. Future research should examine whether the therapeutic effects are long-lasting, whether they are experienced by all COPD patient groups, and which frequency or type of NMES delivers the most effective results.

Keywords: *pulmonary rehabilitation, neuromuscular electrical stimulation, physiotherapy, chronic obstructive pulmonary disease*

Introduction

Chronic obstructive pulmonary disease (COPD) is defined as a preventable and treatable condition/disease characterized by airflow limitation. Although COPD affects the lungs, it also produces significant systemic consequences (Viegi et al., 2007). COPD produces inactivity, which leads to deconditioning, mainly caused by breathing. This leads to an increased fear of exertion and avoidance of physical activities and social activities, trapping the patient within a vicious circle leading to further isolation and depression, accompanied by reduced quality of life (Corhay et al., 2014). Currently, COPD is perceived not only as a pulmonary disease, but more as a systemic disease that affects the functioning of other organs, including the locomotor system. Skeletal muscle dysfunction is among the most common extra pulmonary manifestations of COPD (Kucio et al., 2016).

Pulmonary rehabilitation (PR) is a comprehensive intervention. It is based on a detailed patient assessment. The assessment is followed by therapies that include, but are not limited to, exercise treatment, education, and behavior modification, which are designed to improve the physical and emotional states of people with chronic respiratory disease (Gloeckl et al., 2013). The main components of PR include treatment with exercises, psychosocial and nutritional support, as well as

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education. The exercise program includes two main components: endurance treatment (continuous or with intervals) and strength treatment (Gloeckl et al., 2013; Corhay et al., 2014).

The application of physical therapy in patients with COPD is safe and beneficial (Neder et al., 2002). Recently, Neuromuscular Electrical Stimulation (NMES) has been successfully used as a localized training modality in severely disabled patients, who are unable to follow formal PR and/or tolerate higher training intensities (Nápolis et al., 2011). When COPD symptoms worsen or patients have movement disorders making it impossible for them to perform traditional physical exercises, NMES of the lower limbs can be used as an alternative to traditional physical training. NMES can be used safely on COPD patients when their symptoms get worse, when their disease is advanced, or even while they are receiving respiratory treatment (Kucio et al., 2016). NMES training is more likely to be beneficial for inactive patients with advanced illness than for active patients with stable symptoms and healthy individuals. This is due to the quadriceps muscles, which NMES primarily targets. Being extensively involved in various everyday tasks makes NMES less responsive to improvements in active people. Therefore, NMES treatment is especially advantageous for patients who are unable or unwilling to engage in daily activities or consistent physical activity (Veldman et al., 2016). The efficacy of this technique has not yet been fully demonstrated in patients with COPD (Neder et al., 2002). Implementation of NMES has been associated with increase in muscle strength, functional capacity, and health status in COPD patients (Vieira et al., 2014). NMES appears to be an effectual means of enhancing quadriceps strength and exercise capacity in moderate-to-severe COPD patients (Chen et al., 2016). Based on a meta-analysis reporting equivocal findings about the effects of NMES on COPD patients (Pan et al., 2013) we believe there is a need for further highlighting the effect of NMES on peripheral muscle strength and exercise tolerance in COPD patients. Therefore, the main purpose of this review paper was to evaluate the effectiveness of NMES in the management of COPD patients. In particular, the effect of NMES on peripheral muscular strength and exercise tolerance needs to be investigated.

Methods

Search Strategy

As part of this literature review, seven studies conducted between 2004 and 2022 were considered. All these studies primarily focused on the use of NMES in COPD patients. Figure 1 describes the different phases of the search process. These studies included the following databases: Physiotherapy Evidence Database (PEDro), Google Scholar, and PubMed. They used keywords such as pulmonary rehabilitation, neuromuscular electrical stimulation, physiotherapy, and chronic obstructive pulmonary disease. This search was adapted for searching other databases as well. Based on the information found in the titles and abstracts, a first selection of articles was made using some generalized inclusion criteria. Then, a final selection was made according to an individual critical assessment of the quality of the studies. The assessment was carried out using the PEDro scale, which assesses the validity of each study (Table 1).

Inclusion Criteria

Study inclusion criteria included the following: RCT studies, studies with adult participants (>18 years) diagnosed with COPD, studies involving NMES treatment, English-language studies, free studies, and studies with specific measurements.

Exclusion Criteria

Exclusion criteria included the following: literature review studies, studies carried out prior to 2002, and case studies.

Results

Quality of the Studies

Of all seven studies included in this systematic review, 4 studies showed fair quality (4-5), and 3 studies showed good quality (6-8), which is shown in Table 1.

Table 1. Quality Assessment Using the PEDro Scale

	Items by Number on the PEDro Scale											
Article	1	2	3	4	5	6	7	8	9	10	11	Total Score
Giavedoni et al. (2012)	Y	Y	N	N	N	N	N	Y	N	Y	Y	4
Vieira et al. (2014)	Y	Y	N	Y	N	N	N	N	N	Y	Y	4
Abdellaoui et al. (2011)	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Nápolis et al. (2011)	Y	Y	N	N	Y	N	Y	Y	N	Y	Y	6
Neder et al. (2002)	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Kucio et al. (2016)	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Maddocks et al. (2016)	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8

Note. N: criterion not fulfilled; Y: criterion fulfilled; 1: eligibility criteria were specified; 2: subjects were randomly allocated to groups or to a treatment order; 3: allocation was concealed; 4: the groups were similar at baseline; 5: all subjects were blinded; 6: all therapists were blinded; 7: all assessors were blinded; 8: measures of at least one key outcome were obtained from over 85% of the subjects who were initially allocated to groups; 9: intention-to-treat analysis was performed on all subjects who received the treatment or control condition as allocated; 10: the results of between-group statistical comparisons are reported for at least one key outcome; 11: the study provides both point measures and measures of variability for at least one key outcome; total score: each satisfied item (except the first) contributes 1 point to the total score, yielding a PEDro scale score that can range from 0 to 10

Selection and Characteristics of Studies

A search of electronic databases and scanning the reference lists yielded 65 studies. Lastly, a total of 7 full-text studies were included in the systematic review. The study selection process is shown in Figure 1.

These seven studies included in the systematic review were presented in Table 2. Scientific studies selected for detailed analysis usually had one experimental and one control group. The study results are presented in a table 2.

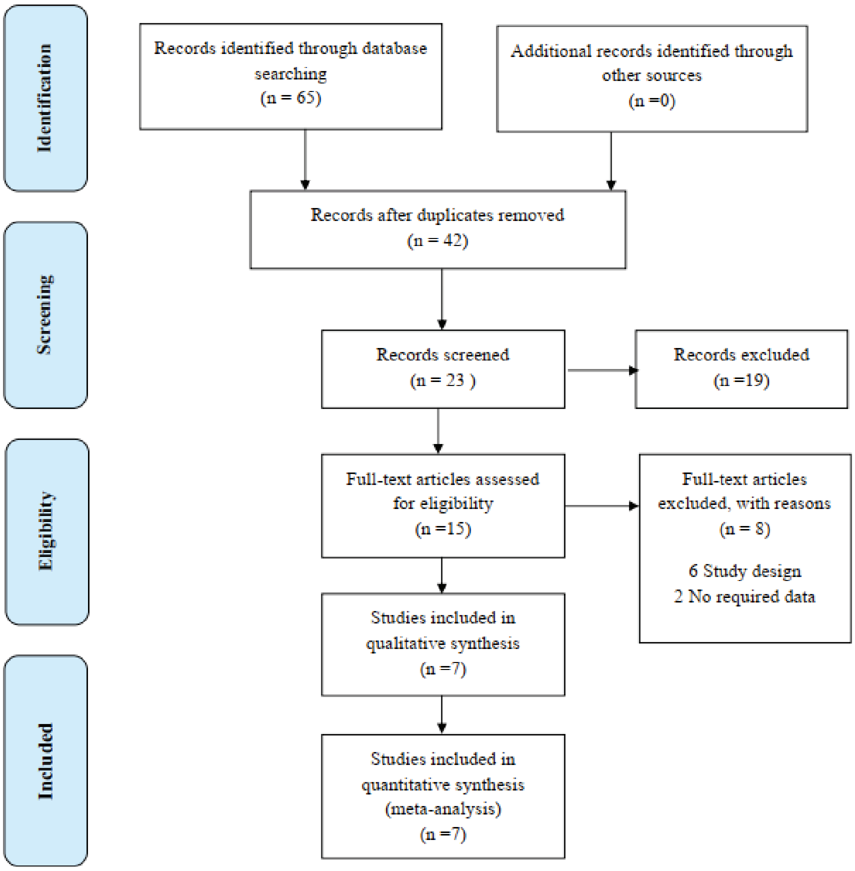

FIGURE 1. PRISMA Study Flow Diagrams

Table 2. Review of Studies

Author / Year /	Population	Experimental Group	Control Group	Measurements	Results
Giavedoni et al., (2012)	N = 11, patients <75 years old with COPD	Standard treatment + NMES on one leg, once a day for 14 days, 50 Hz, pulse duration of 400 ms, 30 minutes	Standard treatment without NMES	QMVC	Mean quadriceps muscle strength increased in the stimulated legs(p < 0.05).
Vieira et al.,(2014)	N = 20, patients <69 years old with stable COPD	NMES 5 times a week, twice a day for 8 weeks, 60 min per session + respiratory therapy, and stretching exercises	Respiratory physical therapy and regular stretching exercises for 8 weeks	Tlim and 6-minute walk test	NMES improves exercise tolerance in patients with COPD.
Abdellaoui et al., (2011)	N = 15, patients <75 years old with acute exacerbated COPD	Weekly sessions of therapeutic education, daily active-passive mobilization, and 35 Hz NMES for 1 hour per day; 5 days per week for 6 weeks	Weekly sessions of therapeutic education, daily active-passive mobilization, and sham electrostimulation	QMVC, 6-minute walking test	QMVC was improved with a significant increase only in the NMES group. Changes in the 6-minute walking distance were also noted, with a significant increase in the NMES group.
Nápolis et al., (2011)	N = 30, patients <70 years old with stable COPD	NMES, with frequency 50 Hz, pulse duration 300-400ms, initial amplitude 15-20 mA, increasing up to 60 mA; Duration: 15 minutes the first week, 30 minutes the second week and then 60 minutes, 5 times a week, for 6 weeks	Sham NMES, with a frequency of 50 Hz, pulse duration of 200 ms, sham stimulation was applied to each leg for 15 minutes, 3 times a week for 6 weeks	Tlim	Exercise capacity was significantly improved in the NMES group.

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Table 2. Review of Studies

Author / Year /	Population	Experimental Group	Control Group	Measurements	Results
Neder et al., (2002)	N = 15, patients <73 years with advanced COPD	Group 1 first received NMES. It was assessed twice (before and after NMES). The treatment period was consistent with the duration shown to be effective in the NMES studies.	Group 2 received NMES after a control period. It was evaluated three times (before and after the 6-week control period and after another 6-week period of NMES).	Peripheral muscle strength and endurance; Tlim	Improvements post NMES were found in the endurance capacity of Tlim and maximal isokinetic strength; but, in isometric mean force and other indices of muscle endurance, they did not reach statistical significance (p>0.05).
Kucio et al., (2016)	N = 30, <75 years old with COPD	NMES 35Hz. + pharmacological treatment+ PR	In addition to pharmacological treatment, the patients were treated only with traditional PR.	6-minute walk test	Post-rehabilitation, a significant increase of 6MWT was observed only in the NMES+PR group.
Maddocks et al., (2016)	N = 52, <70 years with COPD.	Self-administered, 6- week program consisting of 30 minutes of daily bilateral NMES in the quadriceps, with a frequency of 50 Hz in 350 µs pulses, range 0–120 mA	Self-administered, 6-week program consisting of 30 min daily bilateral NMES in the quadriceps, with a frequency of 50Hz in 350 µs pulses, range 0–20mA	6-minute walk test, QMVC	Greater improvements were found in the 6MWT distance, in the active NMES group. Also, positive changes in outcomes in QMVC were found at 6 weeks.

Note. N- total number of respondents, Hz- Hertz, ms- millisecond, mA-milliamperes, µs- microsecond, Tlim - the time to the limit of exercise tolerance of constant work rate, QMVC- maximal voluntary quadriceps contraction

Discussion

Peripheral Muscle Strength

In the study by Abdellaoui et al. (2011), the group receiving NMES provided more substantial and meaningful results related to improvement in quadriceps muscular strength after a 6-week program. The control group also saw a little spontaneous recovery in quadriceps strength, albeit the results were not statistically significant (r=0.79, p<0.001). According to Maddocks et al. (2016), treatment with NMES was linked to improvements in the quadriceps muscle's maximum voluntary contraction (QMVC) (p<0.5). Giavedoni et al. (2012) showed that after 14 days of research, muscle power decreased (p=ns) in the control group's legs, whereas it rose (p<0.01) in legs stimulated with NMES. Between the treatment and control groups, there were statistically significant variations in QMVC (p<0.05). Additionally, Nader et al. (2002) concluded that home-based NMES can enhance peripheral muscle strength and endurance, in the form of a new rehabilitative technique.

Exercise Tolerance

According to Neder et al. (2002), implementation of NMES was associated with an increase in whole-body exercise tolerance. The greatest effects, however, were found in resistance capacity and in time to the limit of exercise tolerance of constant work rate (Tlim); these two values were found to be significantly greater post NMES training. The study by Nápolis et al. (2011) concluded that training systematically with the highest NMES intensities improves the exercise capacity of COPD patients. Kucio et al. (2016) observed that, only the NMES + PR group showed a significant increase in walking distance as part of the walking test (6MWT) following rehabilitation. In the NMES + PR group, the increase in walking distance was 24.1 meters, whereas it was only 10.3 meters in the PR group. The study by Abdellaoui et al. (2011) discovered that differences in 6-minutes walking distance were significantly different between groups (p=0.008), with the NMES-treated group covering significantly more distance (p=0.03), and the control group showing only a modest and non-significant improvement (p=0.24). In the study by Maddocks et al. (2016) , the group treated with NMES showed a considerably larger improvement in the distance assessed with the 6MWT test, compared to the control group (p<0.05). The results of this literature review are detailed below, specifying the publications that belong to each of the five categories analyzed (Table 2).

Benefits and Drawbacks of NMES in COPD patients

Various studies have tested the effect of NMES on peripheral muscle strength and exercise tolerance. Most of the studies reconfirm the positive effect of NMES on peripheral muscle strength and exercise capacity. However, studies focused not only on these two goals, but also on other benefits of NMES in COPD patients. According to Wu et al. (2020), NMES was found to be helpful in enhancing exercise capacity. Further, functional capacity rose following NMES therapy in COPD patients, as evidenced by an improvement in dyspnea feeling. In patients with moderate to severe COPD, Chen et al. (2016) found that NMES is beneficial in boosting quadriceps muscle strength and boosting exercise capacity. Regardless of the severity of airway obstruction, Coquart et al. (2016) observed that NMES significantly improves exercise tolerance, depression, and overall health-related quality of life in COPD patients. The 6-minute walking distance and the modified Borg's dyspnea scale had significant pre- and post-test values between and across groups, according to Mahendiran et al.'s (2019) findings. Despite considerable changes in the physical activity index (PAI), it is obvious that the patient's condition significantly improved following NMES combined with traditional PR. Therefore, the importance of combining NMES with traditional PR is being emphasized.

However, some studies question the efficacy of NMES. According to Latimer et al. (2013), six weeks of NMES training in individuals with stable COPD resulted in modest gains in quadriceps strength and thigh mass that, while statistically significant, had little therapeutic importance. According to a research study by Gerovasili (2016), NMES helps patients with severe COPD, who are unable to finish a traditional rehabilitation program, although with temporary benefits. According to Pan et al. (2013), existing scant data suggest that NMES may not be helpful for COPD therapy in terms of enhancing lower limb functioning. However, given the restricted data availability and potential heterogeneity, the findings of this meta-analysis should be evaluated with care.

Limitations of the Study

Finally, our study too has its limitations. First, clinical studies with a low risk of bias were included. There exists heterogeneity among the studies, including the manner of presentation of treatment protocols and tests. Assessment, comparisons between control and intervention groups, as well as study design are the main methodological limitations in the validity of the current findings. Second, studies that focus on a small number of subjects and studies with larger groups are required to confirm and extend our findings. Third, only English-language studies and free studies were reviewed, excluding non-English-language and paid articles. As a future research direction, several studies can be conducted to provide useful evidence of the effectiveness of NMES across different stages of the disease, as well as for the development of standardized NMES treatment protocols for COPD patients.

Conclusions

Evidence from the above-mentioned literature review suggests that NMES treatment for COPD patients has positive effects on peripheral muscle strength and exercise tolerance. The effectiveness of NMES in improving COPD patients' exercise tolerance and peripheral muscle strength has been highlighted in this review. RCT and other studies with high-quality, evidence-based data are necessary for drawing firmer conclusions about the efficacy of NMES. Future research should examine whether the therapeutic effects are long-lasting, whether they are experienced by all COPD patient groups, and which NMES treatment protocol delivers the best results.

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Conflict of Interest
The authors declare that there are no conflicts of interest.

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