

Jacobs Journal of Pulmonology

Review Article

Why to Buy a Neuromuscular Electrical Stimulator on a Pulmonary Rehabilitation Premise in Less Developed Countries?

Laura D Ciobanu^{*1} MD, PhD, FERS, Dragica P Pesut² MD, PhD, Govind N Srivastava³ MD, PhD

¹University of Medicine and Pharmacy "Gr T Popa" Iasi, Clinical Hospital of Rehabilitation Iasi, Romania

²University of Belgrade School of Medicine, Teaching Hospital of Pulmonology, Clinical Centre of Serbia, Belgrade, Serbia

³Govind N Srivastava, Department of Chest & TB, IMS BHU Varanasi, India

*Corresponding author: Dr. Laura Ciobanu, University of Medicine and Pharmacy "Gr T Popa", 16 Universitatii Street, 700115, IASI, Romania, Tel: 0040-754610731; Email: laura.ciobanu@umfiiasi.ro, lauraciobanu@yahoo.com

Received: 07-06-2015

Accepted: 08-17-2015

Published: 08-27-2015

Copyright: © 2015 Laura

Abstract

Among various techniques used in pulmonary rehabilitation programmes, neuromuscular electrical stimulation (NMES) is an affordable, largely applicable and efficient method to improve overall function in patients suffering from a variety of lung disease. Its role in chronic obstructive pulmonary disease has been well established. NMES is accessible and can be easily utilized by physiotherapists and patients. NMES is frequently used in western countries; however, in less developed or low-resource countries clinicians may not be familiar with NMES. The purpose herein is to describe the role of NMES in pulmonary rehabilitation to analyse potential limitations for its use in some countries.

Keywords: Neuromuscular Electrical Stimulation (NMES); Pulmonary Rehabilitation (PR); Chronic Obstructive Pulmonary Disease (COPD)

Abbreviations

COPD: Chronic Obstructive Pulmonary Disease;

PR: Pulmonary Rehabilitation;

NMES: Neuromuscular Electrical Stimulation;

ADL: Activities of Daily Living;

FFM: Fat-Free Mass;

GOLD: Global Initiative for Chronic Obstructive Lung Disease;

ICU: Intensive Care Unit;

FEV1: Forced Expiratory Volume in One Second;

TNF- α : Tumour Necrosis Factor α

Introduction

Pulmonary rehabilitation (PR) is a safe, reliable and affordable intervention in the non-pharmacological treatment of symptomatic patients with chronic lung diseases. The effects of PR in the management of chronic obstructive pulmonary disease (COPD) has been well established; PR improves symptoms, health-related quality of life and exercise capacity [1,2]. Nevertheless, many other obstructive and restrictive pulmonary conditions benefit from the multidimensional PR, in which exercise training is considered to be the cornerstone [1]. Only 20-40% of patients complete an outpatient PR course, and more than half of them do not have a clinically meaningful improvement [1]. The variable response of patients to the PR measures is tremendously influenced by its heterogeneity, the presence and number of comorbidities co-occurring with COPD [3]. In a study published in 2009, Barr and Celli have shown that the median number of comorbidities in COPD patients is nine [4]. For this reason, new therapies are needed to help chronic lung patients cope with their condition; NMES may be an effective intervention.

New Developments in the Conventional PR

COPD is characterized by progressive airflow limitation which results in exercise intolerance and impaired ability to perform activities of daily living (ADL). Moreover, symptoms of dyspnoea and fatigue compound the ability to exercise or complete ADLs. Anthropometric changes such as involuntary bodyweight loss, fat-free mass (FFM) depletion, physical deconditioning [1], and skeletal muscle weakness with ambulation muscle dysfunction and atrophy [5] have become increasingly more frequent.

Treadmill walking and ergometric cycling are recommended exercises during endurance training¹. They are the most effective physical activities to improve the health-related quality of life and exercise capacity¹. In order to enhance the effects on patients with COPD, they have recently been combined with long-acting bronchodilators, supplemental oxygen, inspiratory pressure support and inspiratory muscle training. In persons severely affected by COPD, interval endurance training might be a useful alternative. Resistance training involving both upper and lower limbs has recently been added [1].

Exercise training may increase the daily level of physical activity in combination with some supplements. These may include oral creatine (an ergogenic aid for a better muscle function and mass), anabolic steroids (to support skeletal muscles against endocrinological disturbances), polyunsaturated fatty acids (that positively influence fat-free mass and skeletal muscle function), antioxidant treatment (e.g. N-acetylcysteine) or plasma ghrelin (a novel growth-hormone releasing peptide useful in patients with involuntary bodyweight loss) [1].

For selected cases of COPD with severe dyspnoea or with prolonged respiratory failure, a recent suitable tool is NMES [5,6] although there are specific indications, technical considerations and limitations. NMES is a passive training of specific locomotor muscle groups that is better tolerated than the whole-body exercise in end-stage COPD or in those with severe dyspnoea [6].

Neuromuscular Electrical Stimulation as a Rehabilitative Strategy

Skeletal muscle dysfunction is characterised by the loss of muscle strength and endurance. It is currently recognised as a hallmark of moderate-to-severe COPD. The metabolic changes within muscles are due to systemic inflammation and cachexia [7]. The loss of strength is explained by the loss of muscle mass through a reduction in the cross-sectional area [8] of fibre and atrophy, especially of the anaerobic type-2x fibres [9]. The loss of endurance is associated with loss of muscle oxidative capacity that comes with fibre-type shifting from type 1 aerobic fibres to type 2a and then type 2x [7, 8, 9] and with reduction in mitochondria and oxidative enzymes within both type-1 and type-2 fibres [9]. These changes will lead to physical deconditioning and the likelihood of muscle fatigue [8]. Peripheral muscle weakness, preceding loss of fat-free mass (FFM), is a common complication and independent predictor of mortality in patients with COPD grade III or IV (GOLD) [10].

Skeletal muscle dysfunction may contribute to decreased exercise capacity, excessive ventilation and increased perception of dyspnoea during exhaustive exercises in COPD. The most affected antigravitational-acting muscle to the lower limb is the quadriceps. Quadriceps muscle dysfunction occurs with exhaustive exercises in COPD. Evidence of quadriceps dysfunction include a decreased capillary/fibre ratio, increased muscle lactate dehydrogenase activity, increased plasma lactate levels, fibre-type shift (from type 1 to type 2a/2x glycolytic fibres), reduced oxidative muscle enzyme activity and exercise-induced muscle oxidative stress [1,7,8]. Measurement of muscle bioenergetics during exercise has revealed a reduced aerobic capacity [8].

In 11-26% of moderate-to-severe COPD rehabilitated patients, cachexia, a disproportional loss of FFM, has been reported¹¹. Further work has identified cachexia as an independent predictor of mortality [11]. In addition, 10-15% of normal-weight COPD patients exhibit "hidden" depletion of FFM, a clinical condition named sarcopaenia. In sarcopaenia, the compositional shift appears to be associated with altered regulation of protein turnover with predilection towards whole-body myofibrillar protein breakdown. Enhanced cellular and muscular protein catabolism has also been observed in COPD patients with muscular atrophy [11].

Similar structural and functional changes in skeletal muscles have been reported in persons with COPD, chronic heart failure and chronic renal failure. Muscle weakness and early fatigue are common symptoms in these chronic organ diseases [12]. PR can stabilise or revert some features of skeletal muscle dysfunction in COPD [13].

In severely dyspnoeic COPD patients, Neder et al [6] showed that six-week therapy with NMES applied to the lower limb muscles involved in ambulation improved muscle mass, strength and endurance, whole body exercise intolerance and breathlessness during everyday activities. Further, data suggested that NMES increased quadriceps peak torque, enhanced ability to perform whole body incremental endurance exercise and reduced breathlessness in everyday activities. The advantage of NMES over conventional exercise training in COPD patients lies in the virtual absence of ventilatory stress during passive exercise, due to the small mass of involved muscles. The metabolic response is significantly lower during a NMES session, when compared to a resistance exercise training session in patients with COPD [14].

It has been shown that NMES improves muscle strength [1]. To reach an equivalent rate of strengthening, a higher intensity of muscle contraction should be used during voluntary exercise. This would result in an increased heart rate, especially in elderly patients. A similar degree of muscle contraction might be reached through NMES without increasing cardiovascular effort [5].

In a very recent study, Vieira et al [15] show that using NMES in COPD patients increases exercise performance, quality of life and peripheral muscle function; these effects were coupled with an improvements in pulmonary function, markers of systemic inflammation and pain modulation. Dynamic hyperinflation and leg muscle fatigue are independently associated with exercise limitation in patients with COPD [16]. The study of Karavidas [17] et al has shown that NMES improves peripheral endothelium-dependent vasodilatation in chronic heart failure, thereby facilitating the blood supply to active muscles. Based on this study, Vieira et al [15] hypothesised that enhanced blood delivery mediated through vasodilatation might explain the increased exercise tolerance in COPD.

NMES is used safely and there are no significant side effects. The patients are able to apply it independently after a couple of supervised sessions by the healthcare practitioners. There are people unable to tolerate the sensations produced by the NMES stimulator, 20% as reported by Chaplin et al [18], but the baseline characteristics were not much different between dropouts and completers. Exclusion criteria for NMES are: a neuromuscular disease; joint disorders in hip, leg and/or knee; metal implants in hip, leg and/or knee; cardiac pacemaker or internal cardiac defibrillator [19].

Neuromuscular Electrical Stimulation in Pulmonary Diseases

NMES can be used in preparation for PR in severely dyspnoeic COPD patients. NMES use will enhance skeletal muscle mass and strength [1], thereby preparing the individual for more aggressive rehabilitative measures. In addition to improving muscle performance, exercise tolerance and health status in COPD, NMES also reduces dynamic hyperinflation, TNF- α and β -endorphin levels [15].

NMES is useful in acute exacerbations of COPD where changes in nutrition, metabolic and oxidative capacity, increased inflammation culminate in poor exercise tolerance. Bed rest and oral methylprednisolone treatment may result in a rapid decrease in muscle mass and force [20]. In COPD patients with steroid-induced myopathy, muscular changes are attributed to diffuse fibre atrophy in quadriceps biopsies, mainly affecting fast-twitch fibres [21]. NMES is a feasible intervention to prevent the decline in muscle strength during hospitalization for acute exacerbation of COPD. Studies show the benefits of NMES therapy in COPD exacerbation appear to be independent of the frequency of stimulation [18].

For critically ill patients, muscle retraining is crucial for effective Intensive Care Unit (ICU) rehabilitation; it helps facilitate weaning and improves outcomes at the time of discharge [22]. Rehabilitation of respiratory patients in critically ill persons is complex. Effective rehabilitation must take into considerations such as whole-body muscle weakness secondary to immobilization and assessment of bronco-pulmonary problems requiring chest physiotherapy for bronchial drainage. Muscle retraining is most effective when instituted early to produce increased strength and aerobic capacity of the treated muscles. Studies show that NMES has beneficial effects on oxygen consumption and lower limbs reperfusion in patients lying in bed. The net effect is a reduction of days needed to make the transfer from bed to chair, and in improvement of the perceived quality of life [22]; NMES also leads to a reduction in bedsores, pneumonia and pulmonary embolism⁵.

In bed-bound patients with severe COPD and who are receiving mechanical ventilation, active limb movements combined with NMES improves peripheral muscle strength, reduces respiratory rate and increases the ability of the patients to sit earlier, leading to an improvement of quality of life [5]. It is well known that physical inactivity compromises muscles mass and strength as studies document a decline of 40% in muscle strength after the first week [22]. The associated atrophy is less expressed in the upper limb muscles, still involved in basic activities of daily life (washing, dressing, and eating).

Neuromuscular Electrical Stimulation – A few Considerations

NMES is a simple, non-invasive and low-intensity stimulation targeting at producing an electrical current that induces muscle contraction without ventilatory stress [22]. NMES produces a visible muscle contraction by applying an intermittent electrical current to a superficial peripheral muscle via conductive electrodes placed close to or over the muscle motor points and activating an intramuscular nerve branch [15,23]. An intact motor nerve is essential. The intermittent electrical current will trigger action potentials, depolarise motor nerves, activate muscle fibres and generate the muscle contraction. Stimulating individual skeletal muscles to contract with NMES, when comparing to whole-body exercise training through brisk walking and cycling, has been shown to evoke minimal ventilatory response and dyspnoea [19,22].

Application of NMES may induce an adaptation in the peripheral muscles to optimise their strength, endurance or both. Conditioning the locomotion muscles via NMES seems likely to optimise the exercise capacity [23]. The conductive pads are attached to a pre-programmed stimulation unit, with changeable parameters in order to promote strength or endurance adaptation in the muscle [23]. Both strength and endurance protocols benefit from the high intensity stimulation that will increase the number of stimulated fibres. In this regard NMES differs from voluntary contractions where the muscle fibres are orderly recruited.

Protocols aimed to promote a strength adaptation will comprise few contractions with high-frequency stimulation and the highest tolerable current. A long-contraction period followed by a longer rest is the best formula. The aim of these protocols is to create the greatest force during each and every contraction, the most suitable way to stimulate contractile protein synthesis [23].

Protocols aiming an endurance adaptation will comprise multiple contractions using low-intensity stimulation for prolonged periods of time. Relatively short contractions and short rest periods seem to be the best formula. The target of these repeated contractions is to elevate metabolism and the accumulation of products that stimulate mitochondrial membrane biogenesis. These products are enzyme proteins as citrate synthase (enzyme involved in the citric acid cycle), 3-hydroxyacyl coenzyme A dehydrogenase (enzyme involved in β -oxidation of fatty acids) and succinate dehydrogenase, all significantly reduced in COPD patients [24,25].

NMES electrodes are placed close to or over the motor-points of the lower limb muscles or to the bilateral quadriceps and rarely to the calf muscles [15]. Sillen et al [26] cited several trials where the stimulated muscles were: quadriceps femoris muscles, quadriceps femoris muscles and hamstrings,

quadriceps femoris muscles and calf muscles, quadriceps femoris muscles and gluteus muscles and quadriceps femoris muscles, hamstrings and calf muscles. In the process a training protocol is chosen that maximizes the effects on muscular fatigue.

All trials have used symmetrical biphasic square pulsed current from 10 to 50 Hz. The pulse duration ranged between 200-700 μ s (generally 300-400 μ s) using the highest tolerable amplitude (15-20 mA at the start of the training session, increasing thereafter up to 100 mA). The duty cycle ranged between 2s on/4 s off and 10s on/50s off. The intensity is increased to facilitate a visible strong muscle contraction or to the maximum tolerated level [15,26]. Session times vary from 20 to 120 min and should occur at intervals of once or twice a day for 3 to 7 days a week. The total number of sessions varies with a reported minimum of 24, and a maximum of 70 [26].

NMES in Less Developed Countries

Little evidence exists to determine NMES utilization in different countries. NMES is frequently employed in Western European countries, but there is a paucity of literature related to NMES utility in less developed countries.

In Serbia, according to a study published in 2014, the prevalence of COPD amongst people aged 40-59 years is 5%, and 8.3% in people aged 60 or older [27]. PR programmes do not describe the use of NMES. In India, NMES plays no role in PR either. The prevalence of COPD is of 5.3% in males and 4.18% in females according to a study published in 2013 [28]. Similarly, there is no use of NMES in chronic respiratory patients in Romania, where the prevalence of COPD is 8.13% for people over 40 years according to a study published in 2013 [29].

Formal cost-effectiveness analysis should be performed to assess the feasibility of NMES on PR outcomes before the widespread use of NMES can be recommended, especially in the less developed countries. NMES devices can be purchased for around £500 and a bulk purchase might further reduce this figure [6]. NMES is a safe, inexpensive and reliable method to facilitate rehabilitation in persons with lung disease or as a component of PR. It has a wide range of applications and can be performed in the ICU, general wards, or in an outpatient setting. Finally, NEMS may shorten duration of hospitalization and thereby save money.

Conclusion

NMES is widely used in neurology and orthopaedics. Over the past 15 years, it has become an adjuvant therapy in pulmonary rehabilitation. NMES is safe, inexpensive, reliable, and easy to use adjuvant therapy that can be used in a variety of settings. Application of NMES has been linked to improved muscle strength, functional capacity and health status in COPD patients. NMES might be considered as an efficacious and

feasible complimentary technique, easy to implement in less developed countries to reduce healthcare costs and improve patient quality of life.

Conflict Interests

The authors mentioned above have no declared or perceived conflict of interests.

References

1. Spruit MA, Wouters EF. New modalities of pulmonary rehabilitation in patients with chronic obstructive pulmonary disease. *Sports Med.* 2007, 37(6): 501-518.
2. Franssen FM, Rochester CL. Comorbidities in patients with COPD and pulmonary rehabilitation: do they matter? *Eur Respir Rev.* 2014, 23(131): 131-141.
3. Clini EM, Beghe B, Fabbri LM. Chronic obstructive pulmonary disease is just one component of the complex multimorbidities in patients with COPD. *Am J Resp Crit Care Med.* 2013, 187(7): 1-3.
4. Barr RG, Celli BR, Mannino DM, Petty T, Rennard SI et al. Comorbidities, patient knowledge, and disease management in a national sample of patients with chronic obstructive pulmonary disease. *Am J Med.* 2009, 122(4): 348-355.
5. Zanotti E, Felicetti G, Maini M, Fracchia C. Peripheral muscle strength training in bed-bound patients with COPD receiving mechanical ventilation: effect of electrical stimulation. *Chest.* 2003, 124(1): 292-296.
6. Neder JA, Sword D, Ward SA, Mackay E, Cochrane LM et al. Home based neuromuscular electrical stimulation as a new rehabilitative strategy for severely disabled patients with chronic obstructive pulmonary disease (COPD). *Thorax.* 2002, 57(4): 333-337.
7. Remels AH, Schrauwen P, Broekhuizen R, Willems J, Kersten S et al. Peroxisome proliferators-activated receptor expression is reduced in skeletal muscle in COPD. *Eur Respir J.* 2007, 30(2): 245-252.
8. Mador MJ, Bozkanat E. Skeletal muscle dysfunction in chronic obstructive pulmonary disease. *Respir Res.* 2001, 2(4): 216-224.
9. Sathyapala SA, Kemp P, Polkey MI. Decreased PPAR concentrations: a mechanism underlying skeletal muscle abnormalities in COPD. *Eur Respir J.* 2007, 30(2): 191-193.
10. Swallow EB, Reyes D, Hopkinson NS, Man WD-C, Porcher R et al. Quadriceps strength predicts mortality in patients with moderate to severe chronic obstructive pulmonary disease. *Thorax.* 2007, 62: 115-120.
11. Franssen FME, Sauerwein HP, Rutten EPA, Wouters EFM, Schols AMWJ. Whole-body resting and exercise-induced lipolysis in sarcopaenic patients with COPD. *Eur Respir J.* 2008, 32(6): 1466-1471.
12. Franssen FME, Wouters EFM, Schols AMWJ. The contribution of starvation, deconditioning and ageing to the observed alterations in peripheral skeletal muscle in chronic organ diseases. *Clin Nutr.* 2002, 21 (1): 1-14.
13. Franssen FME, Rochester CL. Comorbidities in patients with COPD and pulmonary rehabilitation: do they matter? *Eur Respir Rev.* 2014, 23(131): 131-141.
14. Sillen MJH, Janssen PP, Akkermans MA, Wouters EFM, Spruit MA. The metabolic response during resistance training and neuromuscular electrical stimulation (NMES) in patients with COPD, a pilot study. *Respir Med.* 2008, 102(5): 786-789.
15. Vieira PJC, Güntzel Chiappa AM, Cipriano G Jr, Umpierre D, Arena R et al. Neuromuscular electrical stimulation improves clinical and physiological function in COPD patients. *Respir Med.* 2014, 108(4): 609-620.
16. Butcher SJ, Lagerquist O, Marciniuk DD, Petersen SR, Collins DF et al. Relationship between ventilatory constraint and muscle fatigue during exercise in COPD. *Eur Respir J.* 2009, 33(4): 763-770.
17. Karavidas AI, Raisakis KG, Parissis JT, Tsekoura DK, Adamopoulos S et al. Functional electrical stimulation improves endothelial function and reduces peripheral immune responses in patients with chronic heart failure. *Eur J Cardiovasc Prev Rehabil.* 2006, 13(4): 592-597.
18. Chaplin EJJ, Houchen L, Greening NJ, Harvey-Dunstan T, Morgan MD et al. Neuromuscular stimulation of quadriceps in patients hospitalised during an exacerbation of COPD: a comparison of low (35 Hz) and high (50 Hz) frequencies. *Physiother Res Int.* 2013, 18(3): 148-156.
19. Sillen MJH, Franssen FME, Delbressine JML, Vaes AW, Wouters EFM, Spruit MA. Efficacy of lower-limb muscle training modalities in severely dyspnoeic individuals with COPD and quadriceps muscle weakness: results from the DICES trial. *Thorax.* 2014, 69(6): 525-531.
20. Spruit MA, Gosselink R, Trooster T, Kasran A, Gayan-Ramirez G et al. Muscle force during an acute exacerbation in hospitalised patients with COPD and its relationship with CXCL8 and IGF-1. *Thorax.* 2003, 58(9): 752-756.
21. Hopkinson NS, Man WD-C, Dayer MJ, Ross ET, Nickol AH et al. Acute effect of oral steroids on muscle function in chronic obstructive pulmonary disease. *Eur Respir J.* 2004,

- 24(1): 137-142.
22. Venturelli E, Crisafulli E, Degli Antoni F, Trianni L et al. Rehabilitation in critically ill patients. *Ann Resp Med*. 2011, 1 (2): 1-7.
23. Hill K, Mathur S, Roig M, Janaudis-Ferreira T, Robles P, Dolmage TE et al. Neuromuscular electrical stimulation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2013, 11: 1-11.
24. Takahashi M, Hood DA. Chronic stimulation-induced changes in mitochondria and performance in rat skeletal muscle. *J Appl Physiol* (1985). 1993, 74(2): 934-941.
25. Mador MJ, Bozkanat E. Skeletal muscle dysfunction in chronic obstructive pulmonary disease. *Respir Res*. 2001, 2(4): 216-224.
26. Sillen MJH, Speksnijder CM, Eterman R-MA, Janssen PP, Wagers SS et al. Effects of neuromuscular electrical stimulation of muscles of ambulation in patients with chronic heart failure or COPD. *Chest*. 2009, 136(1): 44-61.
27. Nagorni-Obradovic LM, Vukovic DS. The prevalence of COPD co-morbidities in Serbia: results of a national survey. *NPJ Prim Care Resp Med*. 2014, 24: 14008. doi: 10.1038/npjpcrm.2014.8.
28. Vijayan VK. Chronic obstructive pulmonary disease. *Indian J Resp Med*. 2013, 137(2): 251-269.
29. Magureanu IL, Furtunescu F. The importance of determining the prevalence of COPD. *Pneumologia*. 2013, 62(4): 239-246.