NEUROMUSCULAR ELECTRICAL STIMULATION AS AN ALTERNATIVE TO PHYSICAL EXERCISE IN PATIENTS WITH COPD

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Patients with chronic obstructive pulmonary disease (COPD) are unable to do physical exercises included into standard pulmonary rehabilitation programs. Neuromuscular electrical stimulation (NMES) is a good alternative for such patients as it does not aggravate shortness of breath. The aim of this work was to assess the effect of short-term NMES of the quadriceps femoris muscle on the physical activity of patients with COPD. Our prospective open randomized study was carried out in 36 patients distributed into two groups. The main group was administered NMES for 10 days. On day 10 clinical and functional parameters, as well as adverse events, were evaluated. On admission to hospital, the groups did not differ in terms of the studied parameters. Following the treatment course, the main group significantly improved their step count and electromyography results (418.5 (86.0; 815.0) vs. 226.7 (48.0; 660.0), $p = 0.02$, and 463.0 (122; 804) vs. 210.5 (64; 481), $p = 0.0001$, respectively). The patients scored much less on the Mmrc and Borg scales and the CAT-test: 22.8 (18.0; 34.0) vs. 28.4 (26.0; 34.0), $p = 0.00007$; 2.7 (2.0; 4.0) vs. 3.1 (3.0; 4.0), $p = 0.03$; and 6.3 (5.0; 7.0) vs. 7.2 (6.0; 9.0), $p = 0.0002$, respectively. No adverse events were registered in the main group. Based on the obtained results, we conclude that short-term NMES of the quadriceps femoris muscle improves physical activity, the quality of life and ability to do physical exercise in patients with COPD providing them with a good alternative to standard rehabilitation programs.

Keywords: COPD exacerbation, skeletal muscle dysfunction, pulmonary rehabilitation, neuromuscular electrical stimulation

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ЭЛЕКТРОМИОСТИМУЛЯЦИЯ КАК АЛЬТЕРНАТИВА ФИЗИЧЕСКОЙ ТРЕНИРОВКЕ У ПАЦИЕНТОВ С ХОБЛ

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Пациенты с обострением хронической обструктивной болезни легких (ХОБЛ) не способны выполнять тренировочные упражнения в рамках программы легочной реабилитации. Альтернативой служит метод электромиостимуляции (ЭМС), поскольку его применение не вызывает усиления одышки у пациента. Целью работы была оценка эффективности краткосрочной ЭМС четырехглавой мышцы бедра на двигательную активность у пациентов с ХОБЛ. В проспективное открытое рандомизированное исследование вошли 36 пациентов, разделенные на две сопоставимые группы. Пациентам в основной группе проводили ЭМС в течение 10 дней. На 10-е сутки регистрировали и сравнивали клинико-функциональные параметры и потенциальные побочные эффекты. Между двумя группами не было отмечено существенных различий в отношении исходных характеристик. По результатам межгруппового анализа, основная группа имела статистически значимые улучшения показателей измерений, выполненных шагомерм и при миографии, равных соответственно 418,5 (86,0; 815,0) против 226,7 (48,0; 660,0) ($p = 0,02$), 463,0 (122; 804) против 210,5 (64; 481) ($p = 0,0001$). Отмечалось значительное снижение баллов при оценке ХОБЛ по CAT-тесту и оценке одышки по mMRC-шкале и по шкале Borg: 22,8 (18,0; 34,0) против 28,4 (26,0; 34,0) ($p = 0,00007$), 2,7 (2,0; 4,0) против 3,1 (3,0; 4,0) ($p = 0,03$) и 6,3 (5,0; 7,0) против 7,2 (6,0; 9,0) ($p = 0,0002$) соответственно. Побочных эффектов в основной группе отмечено не было. На основании полученных результатов можно сделать вывод, что краткосрочная ЭМС четырехглавой мышцы бедра улучшает двигательную активность пациентов, повышая качество жизни и способность выполнять программы легочной реабилитации в последующем, и является альтернативой физическим тренировкам у пациентов с ХОБЛ.

Ключевые слова: обострение ХОБЛ, дисфункция скелетной мускулатуры, легочная реабилитация, электромиостимуляция

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Chronic obstructive pulmonary disease (COPD) is the leading cause of death and morbidity worldwide [1, 2]. Flare-ups that accompany the natural course of COPD seriously affect the prognosis of patients suffering from this condition [2]. It is becoming evident that COPD and especially its severe forms tend to manifest systemically, having a pronounced effect on survival and promoting co-morbidities. Patients with severe COPD are often cachexic. The loss of muscle mass they develop is the result of apoptosis and/or the lack of muscular activity [3, 4]. Flare-ups are characterized by progressing respiratory failure necessitating the use of systemic glucocorticoids, which, in turn, aggravate skeletal muscle wasting. Subsequently, respiratory muscle fatigue sets in, incapacitating the patient. Less physical activity means progressing weakness, which eventually leads to dystrophy and atrophy of skeletal muscles (Fig. 1). One of the largest muscles responsible for motor performance is the quadriceps femoris muscle. Its weakness and atrophy worsen the prognosis and increase the risk of death in patients with COPD [4].

Because of progressing weakness and atrophy of skeletal and respiratory muscles in severe COPD cases, therapy should include a sufficient amount of physical exercise [5, 6]. It is the crucial component of pulmonary rehabilitation. The rehabilitation course normally lasts from 4 to 12 weeks; the golden mean is 6–8 weeks [6]. Pulmonary rehabilitation lasting for at least 4 weeks improves clinical outcomes and statistically significant parameters in patients with COPD, reducing shortness of breath and fatigue and lifting the patient's spirits [7]. However, patients with severe and extremely severe COPD are not ready to engage in high-load physical rehabilitation because of pulmonary failure and general weakness. Neuromuscular electrical stimulation is a good alternative for such patients, serving as a bridge to a more intensive rehabilitation course [7]. Using the St. George's Respiratory Questionnaire and a few dyspnea scales, researchers have shown that a 4-week rehabilitation course based on the electrical stimulation of the quadriceps femoris muscle has a good therapeutic effect on patients with COPD [8].

In this study we aim to assess the efficacy of short-term neuromuscular electrical stimulation of the quadriceps femoris muscle using surface electromyography and pedometer data in patients with severe and exacerbated COPD who are physically unable to participate in standard pulmonary rehabilitation.

METHODS

This prospective randomized open-label comparative cohort study was conducted from September 2016 through February 2018 at the pulmonary unit of the University clinic. We examined a total of 55 patients with exacerbated COPD and pulmonary failure. Of them only 36 had dysfunction of the quadriceps femoris muscle. Those patients were distributed into 2 groups. The main group (n = 18) was treated with short-term neuromuscular electrical stimulation using Compex muscle stimulators (Compex, France). The results were compared pairwise with the performance of the control group (n = 18). The study was carried out in patients with exacerbated COPD clinically established by the presence of at least 2 signs and symptoms: progressing shortness of breath and progressing cough, mucus hypersecretion or increased production of purulent sputum; signs of pulmonary failure accompanied by weakness and inability to engage in physical activity (confirmed by electromyography and pedometer data); dysfunction of the quadriceps femoris muscle (the EMG amplitude registered during the maximum voluntary muscle contraction was < 600 μV). Patients with hyperthermia (febrile and subfebrile body temperature), normal electromyography, pneumonia, mental disturbances that prevented us from establishing a good rapport with the patient, absolute contraindications to neuromuscular electrical stimulation, such as the presence of a pacemaker, epilepsy, arterial pathology of lower extremities, abdominal or inguinal hernias, were excluded from the study. The study was approved by the local Ethics Committee (Protocol 154 dated April 11, 2016). All patients gave their informed consent to participate.

The comparative analysis was based on patients' age, their scores on the mMRC scale (a questionnaire proposed

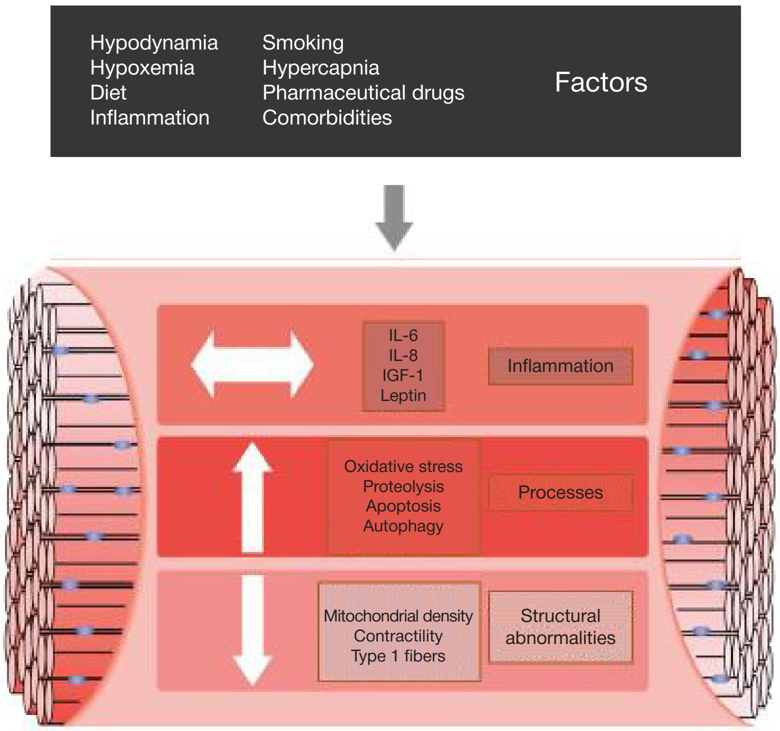

Fig. 1. Factors promoting damage to muscle fibers (Abdulai R. M. et al., 2017.)

by the British medical research council to assess shortness of breath), results of the COPD assessment test (CAT), spirometry data (the forced expiratory volume in 1 s (FEV1) and the ratio of FEV_1/ to FVC), results of the arterial blood gas test (ABG) used to measure pH and partial pressures of oxygen (PaO_2) and carbon dioxide ($PaCO_2$) in arterial blood, and electromyography data collected on admission. All patients received standard treatment for exacerbated COPD as recommended by GOLD guidelines (2017), which included inhaled bronchodilators, systemic corticosteroids (20–40 mg of prednisolone per day), and empiric antibacterial therapy tailored to bacterial sensitivity and coinfections. Clinical characteristics, pedometer data, electromyography findings, scores on Borg dyspnea and mMRC scales, CAT test results, and possible adverse effects were assessed and compared between the groups after 10 days of treatment.

Electromyography

All patients from both groups underwent surface electromyography (EMG), a type of clinical electromyography used to measure the total electrical activity of muscles at rest and effort using skin surface electrodes according to the manufacturer's instructions. Electromyographic signals and evoked potentials were measured using the multifunction Nemus 1 system (EB Neuro, Italy).

Blood collection for ABG

Blood samples were collected from the radial artery at least 15 min after stopping supplemental oxygen using self-filling syringes (PICO70® Radiometer, Denmark); the samples were analyzed on the RAPIDLab® 1200 Systems analyzer (Siemens, Germany) following the manufacturer's instructions.

Pedometer

Physical activity was assessed using the Torneo A-946BTRN pedometer (Compus pro, China). The pedometer was attached to patients' clothing at the waist; measurements were taken for 6 hours in a row when the patient was awake.

Neuromuscular electrical stimulation

The patients from the main groups were prescribed a course of neuromuscular electrical stimulation. The procedure was performed with the patients seated or put in the supine position; patients with severe COPD had a knee pillow placed under their knees. The positive electrode was placed on the skin over the quadriceps femoris muscle in the area of its motor point where the best muscle contraction was achieved under the most comfortable conditions. The negative electrode was placed 10 cm distal to the first. The stimulator was operated in two modes alternating every other day: *Sport| resistance*, 32 min, and *Aesthetic*, *firing*, 22 min. Stimulation intensity was adjusted between 10 mA and 35 mA for each patient based on their tolerance and the induced muscle response.

Statistical data analysis

Statistical data analysis was done in Statistica 10 StatSoft. Nonparametric methods of descriptive statistics were applied;

Table 1. Basic characteristics of the groups

Parameter	Main group (*n* = 18)	Control group (*n* = 18)	*p*
Age, years	66 (53; 77)*	69,6 (53; 80)	> 0,05
Sex, m/f	16/2	15/3	> 0,05
Body mass index, kg/m^2	24,0 (18,3; 31,2)	22,9 (18,1; 27,6)	> 0,05
Smoking index (for smokers), pack-year	45,9 (30; 60)	43,6 (20; 60)	> 0,05
CAT test, points	28,1 (21,0; 39)	30,0 (27,0; 36,0)	> 0,05
Shortness of breath on the mMRC scale, points	3,4 (3; 4)	3,5 (3; 4)	> 0,05
Shortness of breath on the Borg scale, points	8,7 (8,0; 10,0)	8,7 (8,0; 10,0)	> 0,05
FEV_1, %,	31,3 (20; 59)	32,8 (13,0; 56,0)	> 0,05
pO_2, mm HG	58,69 (33,5; 72,4)	59,6 (46,3; 76,9)	> 0,05
pCO_2, mm HG	45,63 (28,6; 65,8)	45,6 (26,1; 74,3)	> 0,05
pH	7,41 (7,36; 7,47)	7,40 (7,38; 7,44)	> 0,05
Surface electromyography of the quadriceps, μV	204,06 (55,1; 435)	194,3 (58; 443)	> 0,05
Pedometer, step count	295 (38,0; 700,0)	220 (45,0; 651)	> 0,05

Note: * — data are presented as Me (Q_1; Q_3); *p* marks statistical significance between the groups.

Table 2. Effect of neuromuscular electrical stimulation in the main group and the controls

Parameter	Main group (*n* = 18)	Control group (*n* = 18)	*p*
Quality of life and SpO_2			
CAT test, points	22.8 (18.0; 34.0)*	28.44 (26.0; 34.0)	0.00007
Shortness of breath on the mMRC scale, points	2.78 (2.0; 4.0)	3.17 (3.0; 4.0)	0.03
Shortness of breath on the Borg, points	6.28 (5.0; 7.0)	7.22 (6.0; 9.0)	0.0002
Saturation of capillary hemoglobin with oxygen, %	93.7 (88.0; 96.0)	93.7 (90.0; 96.0)	0.4
Physical activity and performance of the quadriceps femoris muscle			
Pedometer, step count	418 (86.0; 815.0)	226 (48.0; 660.0)	0.0001
Surface electromyography, μV	463.0 (122.0; 804.0)	210.5 (64.0; 481.0)	0.02

Note: * — data are presented as Me (Q_1; Q_3); *p* marks statistical significance between the groups.

the median (Me), the upper (Q_3) and lower (Q_1) quartiles were computed. The data were presented as (Me (Q_1; Q_3)). To compare two independent samples, the Mann–Whitney U test was used. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Basic characteristics of the patients

On admission, no differences were observed between the patients in terms of the studied clinical characteristics, spirometry findings and electromyography data. ABG tests did not reveal any significant differences in pH, PaO_2, and $PaCO_2$ between the patients (Table 1).

Effect of neuromuscular electrical stimulation on the quality of life

Upon completing the treatment course, the patients assigned to the main group scored less on the mMRC and Borg scales and improved their CAT test results. No significant improvements were observed in the control group (Table 2).

Effect of neuromuscular electrical stimulation on clinical characteristics

The analysis showed that both groups improved their SpO_2 levels; on day 10 no significant differences were observed in SpO_2 levels between the groups (Table 2).

Effect of neuromuscular electrical stimulation on physical activity and the quadriceps femoris muscle performance

The intragroup analysis showed that the main group patients significantly improved their myographic characteristics and step count. Group comparison revealed that those improvements were statistically significant in the main group (Fig. 2. and Fig. 3, respectively) on day 10 (Table 2).

DISCUSSION

Pulmonary rehabilitation is an essential component of the complex therapy of patients with COPD with a particular focus on physical exercise. Pulmonary rehabilitation is evidence-based [2]. However, the question remains as to how we can help those patients with COPD who are unable to join a

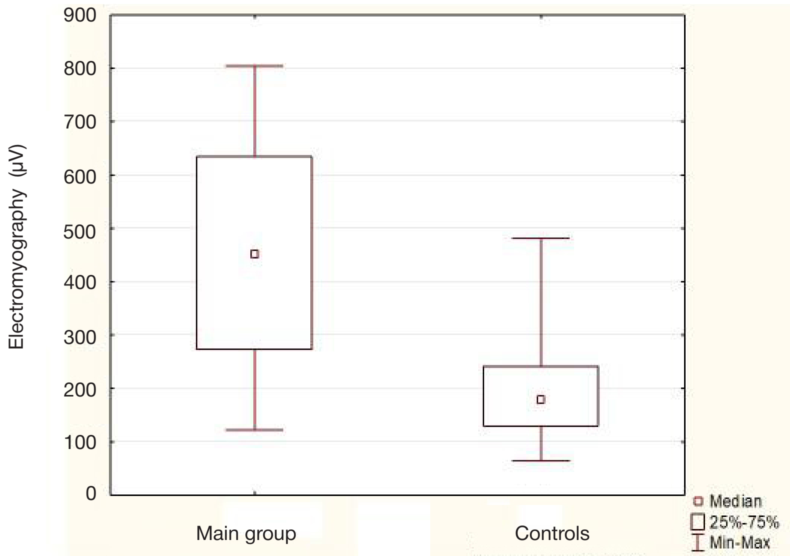

Fig. 2. Electromyography data on day 10 (comparison of two independent samples done using the Mann–Whitney U-test)

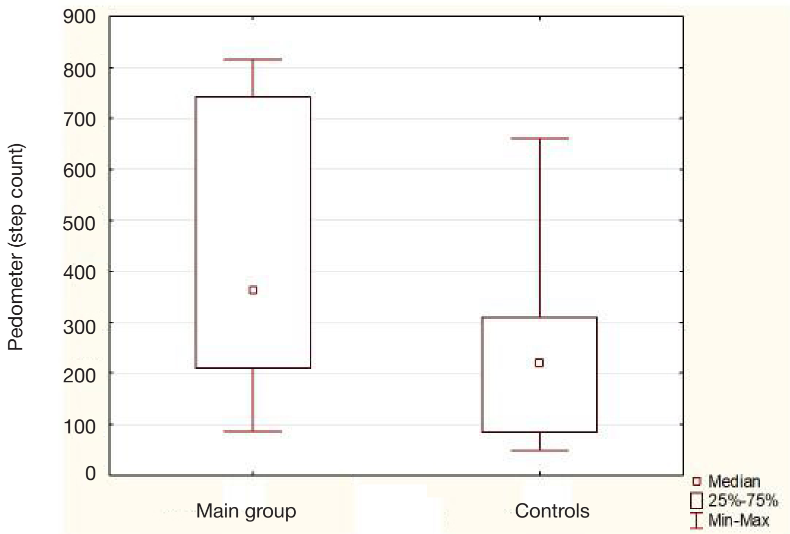

Fig. 3. Electromyography data on day 10 (comparison of two independent samples done using the Mann–Whitney U-test)

standard strength-training program. According to the literature, neuromuscular electrical stimulation can provide a solution for such patients.

So far, only few clinical studies have been carried out investigating the effect of neuromuscular electrical stimulation on the performance of the quadriceps femoris muscle used for the pulmonary rehabilitation of patients with severe forms of COPD [7–10]. In those studies, electrical stimulation was administered over a long period of time, lasting for 4 to 6 weeks, and had a beneficial effect on the patients [11–14]. The method was assessed subjectively using the 6-minute walk test and the St. George's Respiratory Questionnaire [8]. The present study demonstrates that electrical stimulation of the quadriceps femoris muscle rapidly improves its function. The most reliable assessment criterium here is electromyographic data. When analyzing the effect of neuromuscular electrical stimulation on the levels of saturation of capillary hemoglobin with oxygen, we discovered that both groups had increased SpO_2. This may have been the result of the treatment the patients received in parallel, which included bronchodilators and supplemental oxygen (if needed). The main group demonstrated significant improvement of their general health assessed subjectively based on Borg and mMRC scales; this was probably due to decreased shortness of breath following the improvement of the skeletal muscle function. Besides, the number of points scored on the CAT test tended to go down, which is associated with improved physical activity and better quality of life [7].

In our study all subjective changes reported by the patients were confirmed by myography and pedometry data.

CONCLUSIONS

We conclude that neuromuscular electrical stimulation of the quadriceps femoris muscle can become an effective alternative to physical exercise in patients with severe COPD. This method can be used as a component of pulmonary rehabilitation in patients who are unable to engage in intensive physical training.

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