The metabolic response during resistance training and neuromuscular electrical stimulation (NMES) in patients with COPD, a pilot study

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Summary
Resistance training and transcutaneous neuromuscular electrical stimulation (NMES) are new modalities in rehabilitation of severely disabled patients with chronic obstructive pulmonary disease (COPD). The purpose of this study was to compare the metabolic response during resistance training and during NMES of the quadriceps femoris muscles in patients with COPD entering pulmonary rehabilitation.

Pulmonary function, body composition, peak aerobic capacity, the Medical Research Council dyspnoea grade, the one-repetition maximum strength assessment were evaluated in 13 COPD patients. Additionally, peak oxygen uptake, peak minute ventilation and Borg symptom scores were assessed during a resistance training session and a NMES session.

The median peak oxygen uptake and median peak minute ventilation during the resistance training session were significantly higher compared to the NMES session. Additionally, these higher metabolic responses were accompanied by higher symptom Borg scores for dyspnoea and leg fatigue.

To conclude, the metabolic response was significantly lower during a NMES session compared to a resistance exercise training session in patients with COPD. Nevertheless, both modalities seem to result in an acceptable metabolic response accompanied by a clinically acceptable sensation of dyspnoea and leg fatigue.

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The metabolic response during resistance training and NMES in COPD

Introduction

Patients with chronic obstructive pulmonary disease (COPD) experience exercise intolerance, dyspnoea and a decreased health status, in spite of an optimal pharmacological treatment.1

Endurance training alone has been shown to improve health status, exercise tolerance and peripheral muscle function in COPD.2-3 Unfortunately, not every COPD patient is able to complete high-intensity endurance training, such as ergometry leg cycling and treadmill walking, due to exercise-induced dyspnoea and/or muscle fatigue.4,5 Actually, a decreased peripheral muscle force and depletion of muscle mass have been shown to be related to exercise intolerance in patients with COPD, irrespective of the degree of airflow limitation.6,7 It therefore seems reasonable to add new treatment modalities to pulmonary rehabilitation to complement endurance training.8 Resistance training and transcutaneous neuromuscular electrical stimulation (NMES) are new modalities, which have been shown to have positive effects on skeletal muscle function, exercise tolerance and disease-specific health status in patients with severe to very severe COPD, and are well tolerated without creating the overt sensation of dyspnoea.9-12 This is most probably due to a relatively low load on the (severely) impaired respiratory system by exercising a smaller skeletal muscle mass. In fact, resistance training and NMES have even been applied successfully during acute exacerbations of COPD.13-16

Recently, Probst et al.17 have demonstrated a significantly higher metabolic response, defined as oxygen uptake and minute ventilation, during high-intensity endurance training (cycling, walking and stair climbing) in comparison with high-intensity leg press resistance training in COPD. At present, it remains unknown whether and to what extent the metabolic response during NMES is different from the metabolic response during resistance training in COPD. Hence, the purpose of this study was to compare the metabolic response during resistance training and during NMES of the quadriceps femoris muscles in patients with COPD entering pulmonary rehabilitation.

Material and methods

This was a cross-sectional, comparative pilot study. A physiotherapist (MJHS) recruited the patients in the beginning of an inpatient pulmonary rehabilitation programme at the Centre for Integrated Rehabilitation Organ Failure (CIRO) in Horn, The Netherlands as described previously.18 Thirteen elderly patients (seven men) with mild to very severe COPD comprised the study group. All patients were treated with two or more of the following respiratory medications: long-acting \( \beta_2 \)-sympathomimetic (n = 3), selective leukotriene antagonist (n = 1), long-acting parasympatholytic (n = 8), combination of long-acting \( \beta_2 \)-sympathomimetic with inhalation corticosteroids (n = 8), theophylline (n = 3), inhalation corticosteroids (n = 3), mucolytic (n = 6), \( \beta \)-sympathomimetic (n = 3), a combination of parasympatholytic with \( \beta_2 \)-sympathomimetic (n = 1), parasympatholytic (n = 3) and oral glucocorticosteroids (n = 2, both 5mg/day as maintenance therapy).

All procedures were in accordance with the recommendations found in the World Medical Association declaration of Helsinki.19 All patients gave informed consent to take part in the study.

Pulmonary function, body composition (overnight fasting bioelectrical impedance assessment), peak aerobic capacity, peak cycling load, Borg symptom scores for dyspnoea and fatigue (symptom-limited incremental cycle ergometer test), the Medical Research Council dyspnoea grade and the one-repetition maximum strength (1-RM) have been determined as described previously.19

Additionally, all patients had to undergo one session of resistance training of the quadriceps femoris muscles and one session of NMES of the quadriceps femoris muscles on 2 separate days, in random order within the same week, after they were familiarized with the resistance training and NMES.

The resistance training consisted of a bilateral leg extension exercise. The patients were asked to perform three sets of repetitions at a load corresponding with 70% of the predetermined 1-RM (Technogym SpA, Gambettola, Italy). The patients had to rest for 2 min between every session of eight repetitions.

During the NMES, the quadriceps femoris muscles of both legs were electrically stimulated with a portable electrical stimulator (Gymn4, Gymn4 Uniphy N.V., Bilzen, Belgium). A total of eight electrodes were placed on the quadriceps femoris muscles (four on each leg): two on the vastus medialis and two on the rectus femoris muscles and the vastus lateralis muscle. The stimulation protocol consisted of a symmetrical biphasic square pulse at 75 Hz, a duty cycle of 6 s on and 29 s off, a pulse time of 410 μs, intensity adjusted to individual toleration during a session lasting 21 min.

The metabolic response during resistance training and during NMES (e.g. peak aerobic capacity, VO₂; and peak minute ventilation, VE) was determined using an Oxycon Mobile (Viasys Healthcare, The Netherlands). The methodology used to assess the metabolic response has been described in detail elsewhere.17 Additionally, Borg symptom scores for dyspnoea and leg fatigue were obtained before and after both training sessions.

Because the data were not normally distributed, results are presented as median and interquartile range (IQR). For the same reason the Wilcoxon signed ranks test was used to determine differences in VO₂, VE and Borg symptom scores between resistance training and NMES. A priori, the level of statistical significance was set at \( p \leq 0.05 \).

Results

On average, patients had mild-to-severe COPD (GOLD II: n = 6, GOLD III: n = 5 and GOLD IV: n = 2), an abnormal low body mass index, an abnormal low fat-free mass index, poor peak exercise capacity and severe sensations of dyspnoea during daily life (Table 1). None of the patients used supplemental oxygen at rest or during exercise.

The median absolute and relative peak VO₂ during the resistance training session were significantly higher compared to the NMES session. Additionally, median absolute and relative peak VE were significantly higher.
during the resistance training session compared to the NMES session. These higher metabolic responses were accompanied by higher symptom Borg scores for dyspnoea and leg fatigue (Table 2). No serious adverse events occurred during both training sessions.

Discussion

The present pilot study is the first to observe a higher metabolic response, perhaps reflecting higher metabolic demand during a resistance training session than during a NMES session in patients with COPD, accompanied by statistically significant higher Borg symptom scores for dyspnoea and leg fatigue (Table 2).

Resistance training and NMES are two relatively new exercise modalities used in the rehabilitation of (severely) disabled patients with COPD. For example, 8–12 weeks of moderate to high-intensity resistance training has been shown to improve skeletal muscle function, exercise capacity, and disease-specific health status in COPD patients with explicit quadriceps femoris muscle weakness.\(^\text{20,21}\) Moreover, 4–6 weeks of NMES of the quadriceps femoris muscles resulted in improved muscle function, exercise capacity, and disease-specific quality of life among COPD patients who had an abnormal body composition or who were too dyspnoeic to leave their home, respectively.\(^\text{11,21}\) Finally, NMES have even resulted in faster mobilization from bed to chair in bed-bound COPD patients requiring prolonged mechanical ventilation.\(^\text{16}\) Based on the above-mentioned findings, it seems reasonable to conclude that both modalities may be beneficial for COPD patients. Indeed, the findings of this study provide an additional rationale to apply both modalities in COPD patients who are severely disabled by their dyspnoea. In the present study, median peak VO\(_2\) and median peak VE were low to moderate during a NMES session or a resistance training session, respectively, compared to peak VO\(_2\) and peak VE obtained during a symptom-limited incremental cycle ergometer test.\(^\text{15}\) Probst et al.\(^\text{15}\) have found comparable results for a resistance training session in COPD patients during outpatient rehabilitation. Indeed, the metabolic response during endurance exercises has been shown to be significantly higher than resistance training in COPD.\(^\text{17}\)

Also, both NMES and resistance training appear to be applicable during acute COPD exacerbations, which are known to be associated with decline in functional status.\(^\text{13,14}\)

Both resistance training and NMES are well tolerated and lead to acceptable levels of dyspnoea and fatigue in COPD (Table 2). In this study, both training sessions were completed by all volunteering participants and did not result in serious adverse events or complaints of muscle soreness or dyspnoea. Indeed, the biphasic current, which has been shown to produce high values for maximally

### Table 1 Characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median</th>
<th>Interquartile range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>65</td>
<td>55–75</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>52.5</td>
<td>49–66</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>18.7</td>
<td>16.9–23.6</td>
</tr>
<tr>
<td>FFMI (kg/m(^2))</td>
<td>13.7</td>
<td>13.3–14.9</td>
</tr>
<tr>
<td>FEV(_1) (% pred)</td>
<td>49</td>
<td>33–57</td>
</tr>
<tr>
<td>FEV(_1)/VC (% pred)</td>
<td>53</td>
<td>40–65</td>
</tr>
<tr>
<td>DLCO (% pred)</td>
<td>47.5</td>
<td>36–64</td>
</tr>
<tr>
<td>MRC dyspnoea (grade)</td>
<td>4</td>
<td>3–5</td>
</tr>
<tr>
<td>Peak load CPET (W)</td>
<td>49</td>
<td>35–74</td>
</tr>
<tr>
<td>Peak load CPET (% pred)</td>
<td>42</td>
<td>31–67</td>
</tr>
<tr>
<td>Peak VO(_2) CPET (ml/min)</td>
<td>775</td>
<td>586–1112</td>
</tr>
<tr>
<td>Peak VO(_2) CPET (% pred)</td>
<td>50</td>
<td>36–70</td>
</tr>
<tr>
<td>Peak VE CPET (l)</td>
<td>40</td>
<td>28–46</td>
</tr>
<tr>
<td>Peak VE CPET (% MVV)</td>
<td>85</td>
<td>62–104</td>
</tr>
<tr>
<td>Peak HR CPET (bpm)</td>
<td>127</td>
<td>112–133</td>
</tr>
<tr>
<td>Peak HR CPET (% pred)</td>
<td>77</td>
<td>75–85</td>
</tr>
<tr>
<td>Borg dyspnoea CPET (points)</td>
<td>7</td>
<td>4–8</td>
</tr>
<tr>
<td>Borg fatigue CPET (points)</td>
<td>7</td>
<td>3–8</td>
</tr>
</tbody>
</table>

BMI = body mass index; FFMI = fat-free mass index; FEV\(_1\) = forced expiratory volume in 1 s; VC = vital capacity; MRC = medical research council dyspnoea scale; peak load = maximum workload; peak VO\(_2\) = peak oxygen uptake in ml/min.; peak VE = peak minute ventilation in litre; peak HR = peak heart rate; bpm = beats per minute; % pred = percentage predicted value; % MVV = percentage maximal voluntary ventilation; CPET = cardiopulmonary exercise test.

### Table 2 Resistance training (RT) versus NMES.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RT</th>
<th>NMES</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting VO(_2) (ml/min)</td>
<td>273 (229–311)</td>
<td>241 (208–283)</td>
<td>0.099</td>
</tr>
<tr>
<td>Peak VO(_2) (ml/min)</td>
<td>497 (443–592)</td>
<td>311 (238–359)</td>
<td>0.001</td>
</tr>
<tr>
<td>Peak VO(_2) (% peak VO(_2) CPET)</td>
<td>57 (45–84)</td>
<td>34 (30–42)</td>
<td>0.001</td>
</tr>
<tr>
<td>Resting VE (l)</td>
<td>14 (12–18.5)</td>
<td>13 (11.5–15)</td>
<td>0.023</td>
</tr>
<tr>
<td>Peak VE (l)</td>
<td>28 (22.0–32.5)</td>
<td>14 (12.5–19.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Peak VE (% MVV)</td>
<td>58 (43–78)</td>
<td>31 (25–37)</td>
<td>0.001</td>
</tr>
<tr>
<td>Borg dyspnoea (points)</td>
<td>3 (2–4)</td>
<td>1 (1–3)</td>
<td>0.005</td>
</tr>
<tr>
<td>Borg fatigue (points)</td>
<td>3 (2.5–5)</td>
<td>2 (0.8–3.5)</td>
<td>0.031</td>
</tr>
</tbody>
</table>

The data shown (median (IQR)) are the results obtained before and after a session of resistance training (RT) or neuromuscular electrical stimulation (NMES) in 13 COPD patients. VO\(_2\) = oxygen uptake in ml/min; % peak VO\(_2\) CPET = oxygen uptake expressed as a percentage of the peak VO\(_2\) obtained at the end of a symptom-limited cardiopulmonary exercise test; peak VE = peak minute ventilation in litre; % MVV = percentage maximal voluntary ventilation.
electrically induced strength was well tolerated. Despite known benefits of both resistance training and NMES in COPD, the present authors do believe, however, that NMES has several major advantages compared to moderate to high-intensity resistance training. First, NMES is feasible in the patients’ home environment. Second, NMES is also applicable in COPD patients who suffer from long-lasting respiratory failure and who are bed-bound. Third, this study is the first to show that quadriceps femoris muscle training using NMES resulted in statistically significantly lower peak VO₂ and peak VE, associated with lower sensations of dyspnoea and fatigue than a resistance training session. As such, patients with COPD whose ventilatory limitation or dyspnoea precludes their participation in endurance or resistance type exercise training may better tolerate NMES. This study had some methodological limitations and selected patient characteristics which may limit the external validity and broad applicability of the present findings: (1) only patients without long-term oxygen therapy were eligible due to the methodology used; and (2) on average patients had an abnormal body composition. Also, this study included a small number of patients with a wide range of COPD severity, and evaluated metabolic responses to NMES and resistance training during only a single session of each. Therefore, it is not possible to draw conclusions as yet regarding the relative metabolic responses over longer periods of training or to identify subpopulations of patients who may benefit particularly from either technique. In conclusion, peak VO₂, peak VE and symptoms of dyspnoea and fatigue were significantly lower during a NMES session compared to a resistance training session among patients with COPD. Nevertheless, both modalities seem to result in an acceptable metabolic response accompanied by a clinically acceptable sensation of dyspnoea and leg fatigue. These findings provide an additional rationale to design extra studies to assess the effects of NMES and resistance training in (severely) disabled patients with COPD.

### Conflict of interest statement

The authors do not have any conflict of interest with the contents of the present manuscript.

### Acknowledgement

The present authors are grateful to the patients to graciously consent to volunteer in the present study.

### References