ORIGINAL REPORT

PATIENTS WITH ACUTE SPINAL CORD INJURY BENEFIT FROM NORMOCAPNIC HYPERPNOEA TRAINING

Siska Van Houtte, PhD1, Yves Vanlandewijck, PhD1, Carlotte Kiekens, MD2, Christina M. Spengler, PhD, MD3 and Rik Gosselink, PhD1,4

From the 1Department of Rehabilitation Sciences, Katholieke Universiteit Leuven, Faculty of Kinesiology and Rehabilitation Sciences, Leuven, 2Physical Medicine and Rehabilitation, University Hospital Pellenberg, Pellenberg, Belgium, 3Exercise Physiology, Institute for Human Movement Sciences, Swiss Federal Institute of Technology and Institute of Physiology, University of Zurich, Zurich, Switzerland and 4Respiratory Rehabilitation Unit, Universitaire Ziekenhuizen Leuven, Leuven, Belgium

Background: Functional loss of respiratory muscles in persons with spinal cord injury leads to impaired pulmonary function and respiratory complications. In addition, respiratory complications are responsible for 50–67% of the morbidity in this population.

Objective: To investigate the effects of normocapnic hyperpnoea training in acute spinal cord injury.

Patients and methods: Fourteen patients were randomized between control (sham) and an experimental normocapnic hyperpnoea training group. Vital capacity, maximal voluntary ventilation, respiratory muscle strength and endurance, respiratory complications and symptoms were evaluated before, after 4 and 8 weeks of training and after 8 weeks follow-up.

Results: Maximal voluntary ventilation, respiratory muscle strength and endurance improved significantly in the experimental group compared with the control group (p < 0.05). Improvements in vital capacity tended to be different from the control group at 8 weeks of training. The Index of Pulmonary Dysfunction decreased after 4 weeks of training and respiratory complications were reported less frequently in the experimental group compared with the control group.

Conclusion: Normocapnic hyperpnoea training in patients with spinal cord injury improved respiratory muscle strength and endurance. Respiratory complications occurred less frequently after training.

Key words: respiratory muscle training, randomized controlled trial, paraplegia, quadriplegia.


Correspondence address: Rik Gosselink, Respiratory Rehabilitation and Respiratory Division, University Hospital Gasthuisberg, Herestraat 49, BE-3000 Leuven, Belgium. E-mail: rik.gosselink@faber.kuleuven.be

Submitted February 5, 2007; accepted September 7, 2007.

INTRODUCTION

Functional loss of respiratory muscles in persons with spinal cord injury (SCI) results in decreased inspiratory and expiratory muscle strength (1, 2), impaired pulmonary function (3–5) and decreased rib cage and pulmonary compliance (1, 6, 7). It is well established that respiratory complications, probably resulting from impaired pulmonary function, account for a large proportion of mortality (8, 9) and morbidity (8, 10). As respiratory muscle atrophy and subsequent impaired pulmonary function are caused not only by denervation of respiratory muscles, but also by inactivity and deconditioning, respiratory muscle training might be an interesting option for treatment. A systematic review concluded that respiratory muscle training tended to improve expiratory muscle strength, vital capacity and residual volume, but insufficient data were available to make conclusions concerning the effects on inspiratory muscle strength, respiratory muscle endurance, quality of life, exercise performance and respiratory complications (11). As both inspiratory and expiratory muscle function is impaired in SCI, and separate training of either of these muscle groups suggests positive effects (11), normocapnic hyperpnoea, inducing concomitant training of inspiratory and expiratory muscles, may be an attractive training modality in these patients. Furthermore, as respiratory muscles normally work at low resistance – challenging respiratory muscles by forced hyperpnoea rather than high resistance seems to be the more “natural” way of training these muscles. Indeed, normocapnic hyperpnoea training has already shown to improve respiratory muscle endurance, expiratory muscle strength and the physical component of the short form-12 health survey in patients with chronic obstructive pulmonary disease (12).

The aims of the present study were, therefore, to investigate the effects of normocapnic hyperpnoea training on pulmonary function, respiratory muscle strength and endurance, as well as on the incidence of respiratory symptoms in acute SCI.

MATERIAL AND METHODS

Patients

Patients hospitalized from November 2002 until September 2004 in the Department of Rehabilitation of the University Hospital Pellenberg, Belgium, who met the following inclusion criteria were retained for the study: (i) acute SCI with lesion level between C4 and T11; (ii) time between lesion and inclusion in the study at least 6 weeks; (iii) American Spinal Injury Association (ASIA) impairment classification.
Table I. General characteristics of patients in control group (n = 7) and experimental group (n = 7)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>Gender</th>
<th>FVC (% predicted)</th>
<th>PImax (% predicted)</th>
<th>PEmax (% predicted)</th>
<th>Duration of injury (months)</th>
<th>Lesion level</th>
<th>ASIA</th>
<th>C/I</th>
<th>Smoking</th>
<th>Mechanical ventilation (days)</th>
<th>Intensive care (days)</th>
<th>Injuries or complications related to breathing prior to training</th>
</tr>
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<tbody>
<tr>
<td><strong>Control group</strong></td>
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<tr>
<td>56</td>
<td>55</td>
<td>173</td>
<td>M</td>
<td>36</td>
<td>28</td>
<td>6</td>
<td>3</td>
<td>C4</td>
<td>B</td>
<td>I</td>
<td>No</td>
<td>0</td>
<td>15</td>
<td>Minor respiratory complications#</td>
</tr>
<tr>
<td>66</td>
<td>57</td>
<td>172</td>
<td>M</td>
<td>65</td>
<td>46</td>
<td>12</td>
<td>4</td>
<td>C5</td>
<td>B</td>
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<td>37</td>
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<td>185</td>
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<td>24</td>
<td>6</td>
<td>5</td>
<td>C5/C6</td>
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<td>C</td>
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<tr>
<td>17</td>
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<td>173</td>
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<td>73</td>
<td>69</td>
<td>31</td>
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<td>C</td>
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<td>22</td>
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<td>T9</td>
<td>B</td>
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<td>C</td>
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<td>0</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

*Patients who quitted smoking after injury. #Minor respiratory complications were for example increased cough or sputum.

FVC: forced vital capacity; PImax: maximal inspiratory mouth pressure; PEmax: expiratory mouth pressure (litres/minute). ASIA: American Spinal Injury Association; C: complete injury; I: incomplete injury; M: male; F: female; IQR: interquartile range.
the tube permitted additional inspiratory and expiratory flow. The first step in order to obtain optimal settings for the normocapnic hyperpnoea was to change the size of the bag. In a second phase the size of the hole could optimize the conditions \((\text{CO}_2/\text{O}_2\text{ fraction})\) during normocapnic hyperpnoea \((\text{NCH})\) training by making small changes in the amount of fresh air. This approach was validated in 2 previous studies \((13, 14)\).

During normocapnic hyperpnoea, minute ventilation was displayed to the patient for feedback and a digital metronome paced breathing frequency.

Patients performed the RET until they could not achieve the target ventilation for 10 consecutive breaths despite the encouragement of the investigator. RET trials were repeated \((\text{after at least } 48 \text{ h of rest})\) until a target duration between 7–15 min was reached. If patients were unable to breathe for 7 min during RET, target ventilation was decreased by 5% for the next RET trial. Alternatively, if patients were able to breathe for 15 min or more, target ventilation was increased by 5% for the next trial. The RET was repeated to control for test-retest reliability and revealed no difference between test and retest \((p = 0.925)\). Immediately after exhaustion, patients were asked to rate their level of perceived exertion and shortness of breath by means of a Borg score from 0 to 10 \((15)\). In case the duration of the RET improved to 30 min \((\text{cut-off})\) after 4 weeks of training, a second RET \((\text{RET})\) was performed at a ventilation + 5% after at least 48 h of recovery.

Normocapnic hyperpnoea training

Patients were informed that there were 2 training conditions, “slow and deep breathing” \((\text{control group})\) and “fast and deep breathing” \((\text{experimental group})\). Patients in the control group were unaware of the fact that they served as control patients. Control patients breathed at a constant ventilation of 15% maximal voluntary ventilation \((\text{MVV})\) and a breathing frequency of 15–25 breaths/min \((\text{sham training})\). Patients in the experimental group breathed at a ventilation between 30% and 40% MVV with a breathing frequency between 30 and 45 breaths/min. All patients trained at the prescribed target ventilation for 30 min, 4 times a week, for 8 weeks. If patients in the experimental group could sustain the target for 25 min, the pace of the metronome was increased by steps of 2 breaths/min\((-1)\). Tidal volume was increased, if breathing frequency reached 45. During training, target minute ventilation was displayed to the patient and a digital metronome paced breathing frequency. At least once a week, \(P_{\text{ET CO}_2}\) was controlled during training. Perceived exertion and shortness of breath were assessed at the end of the training session. All training sessions were supervised and training conditions, remarks and intercurrent illnesses were recorded in a diary.

Pulmonary function and respiratory muscle strength

FVC and MVV in 12 sec were measured using a portable device \((\text{Spirobank, Medical International Research, Italy})\) according to ERS guidelines \((16)\). Reference values of Quanjer et al. \((16)\) were used. Maximal inspiratory \((\text{PI}_{\text{max}})\) and expiratory \((\text{PE}_{\text{max}})\) muscle function were evaluated using a modification of the Black and Hyatt \((17)\) technique. An electronic pressure transducer was used to record pressure. The signal was recorded for further evaluation. At least 5 attempts were made both from total lung capacity \((\text{PE}_{\text{tot}})\) and residual volume \((\text{PI}_{\text{res}})\). \(\text{PI}_{\text{max}}\) and \(\text{PE}_{\text{max}}\) were determined as the pressure that could be sustained for more than 1 sec. Tests were repeated until variability between the 3 best attempts was less than 5%. The highest values were presented in percent of the predicted values of Rochester & Arora \((18)\). For all measurements patients were sitting in their wheelchair with the arms relaxed beside the body or on the thighs \((\text{quadruplegia})\).

Respiratory symptoms and complications

Respiratory complications were evaluated at regular visits by an independent physician, who was unaware of the purpose of the study or the allocation of treatment, assessing patients for respiratory symptoms \((\text{e.g. increased cough, sputum, fever})\). Respiratory complications were defined from a clinical perspective. Whenever patients did seek or required additional medical attention for a respiratory symptom, “confirmed” with more objective data as decided by the physician, this was reported as respiratory complication. This definition is in part lent from the definition of an “acute exacerbation” of chronic obstructive lung disease \((19)\).

The subjective feeling of pulmonary dysfunction was evaluated with the Index of Pulmonary Dysfunction developed for patients with multiple sclerosis \((20)\). The index \((4 \text{ is best and 11 is worst})\) consists of patient’s subjective report of his/her ability to cough and to clear pulmonary secretions, and clinical signs \((\text{strength of patient’s cough and ability to count on a single exhalation})\) were rated by the examiner. Similar to patients with multiple sclerosis, patients with SCI have severe impairment of expiratory muscle function resulting mainly in cough impairment and difficulty in clearing pulmonary secretions \((21)\).

Statistics

A power analysis prior to the study was performed on data obtained in a pilot study \((22)\). RET was chosen as primary outcome since the main aim of the study was to improve respiratory muscle endurance. Using a pre-post model with 2 groups, power calculation revealed a power of 1.0 with 9 patients \((\text{control group}: n = 3\), \(\text{experimental group}: n = 6)\).

In order to compare within-group results before and after 4 and 8 weeks of respiratory muscle training, and after 8 weeks follow-up, Friedman’s analysis of variance \((\text{ANOVA})\) \((\text{repeated measures})\) was performed. \(A\ posteriori\), Wilcoxon tests were used to compare matched pairs within a particular group. The Mann-Whitney \(U\) test was used to compare baseline characteristics as well as differences between baseline and 4 weeks, 8 weeks and 16 weeks data between groups. Spearman’s coefficient was used for the single correlation between relevant outcome variables \((n = 14)\). All statistical analyses were performed using Statistica 6.1 \((\text{Statsoft, Inc., Tulsa, OK, USA})\) and results were expressed as median interquartile range \((\text{IQR})\). The level of significance was set at \(p \leq 0.05\) for all analyses.

RESULTS

Patient characteristics

Twenty patients met the criteria, of which 3 refused to participate, while another 3 patients were excluded between test day 1 and 3: one due to severe cognitive problems, one because of hampering spasticity in lower limbs and one patient refused after having started. This total of 14 patients completed the entire training programme. Baseline pulmonary function and respiratory muscle strength are presented in Table I. There were no differences between patients in the control and experimental group concerning age, weight, height, level and duration of injury, days with mechanical ventilation or stay on intensive care, pulmonary function and respiratory muscle strength. Only \(\text{PI}_{\text{max}}\) tended to be higher in the experimental group compared with the control group \((p = 0.085)\).

Training conditions

Patients in the control and experimental group completed an average of 27 \((\text{standard deviation (SD) 2})\) and 28 \((\text{SD 3})\) \((\text{sham})\) training sessions, respectively \((\text{maximal feasible number of training sessions} = 32)\). This resulted in a patient compliance of 86% \((\text{SD 3})\) and 88% \((\text{SD 10})\) in the control and experimental group, respectively. In both groups intercurrent illnesses \((\text{such as bladder infection, low blood pressure, headache or influenza})\)
were the main reasons for short interruptions of the protocol. All sessions were recovered by the end of the programme. In general, patients perceived the training sessions as positive without special complaints. One quadrupleptic patient in the experimental group complained of neck pain due to spasm of the neck muscles.

Target minute ventilation in the control group remained constant over the training period with a ventilation of 15 (SD 6) l/min (15 (SD 4) % MVV). Target minute ventilation in the experimental group increased significantly from 35 (SD 13) l/min (30 (SD 8) % MVV) to 49 (SD 18) l/min (40 (SD 11) % MVV) after 8 weeks of training \( (p = 0.043) \). \( P_e\text{CO}_2 \) during training was 33 (SD 5) mmHg (control group) and 35 (SD 4) mmHg (experimental group) and did not differ from resting breathing, i.e. 36 (SD 5) mmHg and 37 (SD 3) mmHg, respectively.

Effects of training

**Pulmonary function and respiratory muscle strength** (Table II). In control patients, pulmonary function or respiratory muscle strength did not change at any point in time. In contrast, in the experimental group Friedman ANOVA revealed significant differences for FVC \( (p = 0.021) \), MVV \( (p = 0.054) \), \( \text{PI}_{\text{max}} \) \( (p = 0.011) \) and \( \text{PE}_{\text{max}} \) \( (p = 0.0473) \). Trends for improvement were found after follow-up for FVC \( (+15 (14) \%, p = 0.075) \) and MVV \( (+13 (21) \%, p = 0.091) \). Between-group analyses also revealed significant differences, whereas a trend was observed for improved FVC and \( \text{PI}_{\text{max}} \) \( p = 0.06 \). In addition, \( \text{PE}_{\text{max}} \) failed to improve after 4 weeks of training \( (p = 0.093) \).

**Respiratory endurance.** Changes in duration of RET following (sham) training are presented in Fig. 1 and Table II. RET duration did not change significantly over time in the control group, while RET duration of the experimental group improved significantly \( (p = 0.001) \) by 256 (121) % \( (p = 0.018) \) after 4 weeks of training already (all but one subject reached the 30 min cut-off duration). The improvement (i.e. maximal duration) remained after 8 weeks of training \( (+259 (93) \%, p = 0.018) \) compared with baseline, as well as after follow-up \( (+231 (108) \%, p = 0.018) \). This resulted in significant differences of RET duration between groups after 4 \( (p = 0.009) \) and 8 weeks of training \( (p = 0.003) \), as well as after follow-up \( (p = 0.002) \).

Improvements in MVV correlated significantly with changes in FVC \( (r = 0.678), \text{PI}_{\text{max}} (r = 0.662), \text{PE}_{\text{max}} (r = 0.574) \) and RET \( (r = 0.538) \) after 4 weeks of (sham) training in both groups. After 8 weeks of training, MVV correlated significantly with FVC and RET (Fig. 2).

**Respiratory symptoms and complications.** After 4 weeks the Index of Pulmonary Dysfunction changed from 7.7 (2.7) towards 8.1 (2.0) in the control group and from 7.9 (1.5) towards 7.1 (1.4) in the experimental group. Between-group comparison at 4 weeks revealed a significant improvement in favour of the experimental group \( (p = 0.030) \). This improvement failed to remain at 16 weeks \( (p = 0.074) \). The incidence of respiratory symptoms and complications is presented in Table III.

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**Table II. Pulmonary function and respiratory muscle strength before and after 4 and 8 weeks of (sham) training and after follow-up (16 weeks) in the control and experimental group**

<table>
<thead>
<tr>
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<th>Control group</th>
<th>Experimental group</th>
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<tbody>
<tr>
<td></td>
<td>Before</td>
<td>4 weeks</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>3.8 (2–4.3)</td>
<td>3.6 (2.3–3.9)</td>
</tr>
<tr>
<td>MVV (l/min)</td>
<td>93 (72–145)</td>
<td>84 (65–113)</td>
</tr>
<tr>
<td>( \text{PI}\text{max} ) (cmH2O)</td>
<td>-54 (41–73)</td>
<td>-60 (44–65)</td>
</tr>
<tr>
<td>( \text{PE}\text{max} ) (cmH2O)</td>
<td>46 (19–50)</td>
<td>34 (17–42)</td>
</tr>
</tbody>
</table>

Values are expressed as median (IQR). \(*p < 0.05\) for within-group differences, †\( p < 0.05\) for between-groups differences, ‡\( p < 0.01\) for between-groups differences compared with baseline.

FVC: forced vital capacity; MVV: maximal voluntary ventilation, in 12 sec; \( \text{PI}\text{max} \): maximal inspiratory mouth pressure; \( \text{PE}\text{max} \): expiratory mouth pressure.

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tended to be lower in the control group, inviting towards a regression to the mean phenomena after the training. However, the experimental group improved statically significantly better than the control group.

Training effects

Pulmonary function and respiratory muscle strength. A tendency for improved FVC (20%) was present at 8 weeks of training. Liaw et al. (23), providing inspiratory muscle training in SCI, observed larger improvements (50%) in the experimental group (23). No between-group differences were found probably due to lack of power in both studies. In contrast, the controlled trial of Gounden (24) in 40 persons with quadriplegia (C5–C8) showed improved vital capacity compared with controls after 8 weeks of expiratory muscle training. The statistically significant improvement in MVV affirms the findings of NCH training in healthy individuals (25, 26). It is suggested that the tendency for improvement in FVC as well as the improved respiratory muscle endurance of the present study contributed to the improvements in MVV. The correlations between the improvements in MVV and FVC and between MVV and RET further support this suggestion (Fig. 2).

The improvements in PE\textsubscript{max} are in agreement with the findings of Gounden (24). The changes in PE\textsubscript{max} are likely to be related to training of secondary respiratory muscles. Indeed, Fujiwara et al. (27) provided electromyographical evidence that m. pectoralis major and m. latissimus dorsi play an important role in expiratory function in quadriplegia. In addition, Estenne & De Troyer (28) showed that the clavicular part of the m. pectoralis in quadriplegia plays a major role during coughing and therefore may be recruited during active expiration. They showed that training of the m. pectoralis improved m. pectoralis strength (29).

Respiratory muscle endurance. Our observation of a large improvement in respiratory muscle endurance is in agreement with other studies where healthy individuals received respiratory muscle endurance training by means of isocapnic hyperpnoea (25, 26, 30–32). Uijl et al. (33) and Loveridge et al. (34) found an improved respiratory muscle endurance after respiratory endurance training of the inspiratory muscles in SCI, but no between-group differences was revealed.

Improvements in endurance capacity are expected from (hyperpnoea) training characterized by high number of repetitions with low external load (25, 35). Ramirez-Sarmiento et al. (36) showed an increase in proportion of the type 1 fibres in the external intercostal muscles following inspiratory muscle training in chronic obstructive pulmonary disease. Also Bisschop et al. (37) showed significant hypertrophy of type 2a fibres in the diaphragm after low intensity endurance inspiratory resistive training in rats. These specific cellular adaptations of the respiratory muscles might explain the improved endurance capacity observed in the present study.

Respiratory symptoms and complications. The Index of Pulmonary Dysfunction was lower (i.e. improvement) compared with control patients after 4 weeks of training. The improved

DISCUSSION

The present data show that MVV, inspiratory and expiratory muscle strength and respiratory muscle endurance improved during 8 weeks of NCH training in acute patients with SCI. Vital capacity tended to be different from the control group at 8 weeks of training, while the Index of Pulmonary Dysfunction significantly improved after 4 weeks of training. Finally, respiratory complications were reported less frequently in the experimental group compared with the control group.

Limitations of the study

Although over 70 patients were hospitalized over a period of almost 2 years, our inclusion criteria lead to the exclusion of 56 patients. Most of these exclusions (n = 35) were due to admission for chronic SCI or lower than T11 lesions. The study was well powered for the primary outcome, but was probably underpowered to obtain statistical significant differences following training for all variables. The small sample size of the study did not allow conclusions concerning the impact of lesion level on the benefits of NCH training. Baseline PI\textsubscript{max}

Table III. Incidence of respiratory complications in control (14 episodes) and experimental (1 episode) group during the course of the study

<table>
<thead>
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<th>Control group (n = 7)</th>
<th>Experimental group (n = 7)</th>
</tr>
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<td>1 2 3 4</td>
</tr>
<tr>
<td>Number of subjects</td>
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<td></td>
</tr>
<tr>
<td>with respiratory</td>
<td>3 2 1 1</td>
<td>1 – – –</td>
</tr>
<tr>
<td>complications</td>
<td></td>
<td></td>
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</table>
and respiratory muscle endurance (i.e. RET) might have influenced the ability to cough and the counting on a single exhalation, respectively. This improvement in the Index of Pulmonary Dysfunction may be related to the lower incidence of respiratory complications in the experimental group. It is well established that interventions aiming to reduce pneumonia or atelectasis, generally focus on enhancing secretion removal through assisted-cough techniques (38) and increasing minute ventilation (39, 40). NCH training at levels between 30% and 40% of the MVV in the experimental group offers an adequate alternative to enhance lung expansion and increase flow rates to move secretions.

Alternatively, as presented in Table I, control patients tended to have more respiratory complications prior to training and this might also contribute to the observed differences.

Feasibility of endurance training in acute patients with SCI and clinical implications. NCH training is time-consuming, physically demanding and might load the cardiovascular system. In addition, this mode of respiratory muscle training requires a high level of subject motivation. However, patient’s compliance with training was on average 87%. None of the patients questioned training conditions or asked for adaptations in the training programme. Two experimental patients reported increased spasticity, whereas one patient complained of neck pain due to spasm of the neck muscles. No development of hypercapnia during the entire training programme was observed. Based on the positive outcome of the current study, respiratory muscle training can be recommended to be part of the rehabilitation of patients with a SCI. These patients are more susceptible for atelectasis and hypoventilation and therefore have an increased risk for occurrence of respiratory complications. The findings of the present study indicate that respiratory complications may occur less frequently with respiratory muscle training. In follow up of the successful application in patients with chronic obstructive pulmonary disease (12), respiratory muscle training might also be indicated in patients with chronic SCI. The aim in patients with ventilatory limitation of exercise capacity might be to improve ventilatory function and thus exercise performance.

In conclusion, NCH training in acute SCI improves MVV, inspiratory and expiratory muscle strength and respiratory endurance capacity (i.e. RET). FVC tended to be different following training. The Index of Pulmonary Dysfunction decreased in favour of the experimental group. Finally, respiratory complications occurred less frequently in experimental compared with control patients.

ACKNOWLEDGEMENTS

The authors appreciate the enthusiastic, persistent and voluntary participation of the patients in this study. We are also grateful to the physiotherapists Frank Goditiabois, Bea Slaets and Sofie Jacobs, as well as the nursing staff of the University Hospital Pellenberg.

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