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INSPIRATORY MUSCLE TRAINING IMPROVES BREATHING PATTERN DURING EXERCISE IN COPD PATIENTS

Running Head: Exercise breathing pattern after IMT

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Key words: COPD; inspiratory muscle training; pulmonary rehabilitation; breathing pattern; maximal incremental cycle ergometry test

Take home message

The addition of IMT to a PR program for selected COPD patients resulted in changes in breathing pattern during exercise.

To the Editor:

Dyspnoea is typically the main symptom limiting exercise capacity in patients with chronic obstructive pulmonary disease (COPD) [1-3]. Exertional dyspnoea has been linked to dynamic hyperinflation (DH), when lung expansion critically encroaches upon the inspiratory reserve volume (IRV) [4]. Consequently, patients develop a rapid and shallow breathing pattern, which is energetically opposite to the pattern required to minimise the work of breathing [5]. Furthermore, the restriction of tidal volume (V_T) expansion has recently been linked to daily physical activity limitation [6].

Besides mechanical factors, the limitation on V_T expansion might also be related to an imbalance between the load / capacity relationship of the inspiratory muscles. The inspiratory muscles are functionally weakened by DH during exercise. Furthermore, they are also forced to contract at higher velocities, whilst working against elevated elastic loads [7,8]. These factors might exacerbate restriction of V_T expansion and exacerbate exertional dyspnoea.

Inspiratory muscle training (IMT) is applied in COPD patients during pulmonary rehabilitation (PR) to improve inspiratory muscle function, exertional dyspnoea, and exercise tolerance [9,10]. Wanke et al. previously studied the effects of mechanical threshold loading IMT (MTL-IMT) in addition to general exercise training and observed additional improvements in exercise capacity and larger V_T expansion at peak exercise in the IMT group [10]. We have reported recently that high intensity tapered flow resistive loading IMT (TFRL-IMT) resulted in significantly larger increases in respiratory muscle strength and endurance, as well as changes in breathing pattern during loaded breathing, compared with conventional MTL-IMT [11]. We were led to speculate that the specific characteristics of TFRL-IMT might result in beneficial changes in breathing pattern during whole body exercise [11].

We hypothesised that the addition of TRFL-IMT to a PR program would have the following effects: 1) enhancement of inspiratory muscle function might result in improvements in V_T expansion, by providing a training stimulus within the range of IRV, and 2) enhancement of the velocity of shortening of the inspiratory muscles against high resistances might enable patients to shorten their inspiratory time and leave more time for expiration.

This historically controlled study was approved by the University Hospital Leuven's Institutional Review Board (Approval Number ML7489) and registered at www.clinicaltrials.gov (NCT02186340). Twenty-five clinically stable COPD patients with inspiratory muscle weakness (PImax <100% predicted) gave their written informed consent, and were offered IMT during the final 8 weeks of a 12-week multidisciplinary PR program. A historical control group including patients who participated in an *identical* PR program without IMT was recruited from the PR database of the University Hospital Leuven. These patients were individually matched to the participants of the combined intervention for the following baseline characteristics upon entry into the program: age, gender, pulmonary function, PImax, and exercise capacity.

Patients performed daily high intensity TFRL-IMT (POWERbreathe® KH1, HaB International Ltd., Southam, UK) consisting of two cycles of 30 breaths at the highest tolerable intensity according to a recently published protocol [11].

All repeated measures analyses of changes in breathing pattern at different levels of ventilation were performed in SAS, release 9.3. Levels of ventilation were defined as percentages of baseline maximal ventilation (V_{Emax}) (40, 60, 80, and 100% of peak ventilation of the baseline cycling test). Outcomes between groups were compared with a mixed models analysis. The Tukey method was used to correct post-hoc comparisons between groups at cut-off levels of V_E for multiple testing.

Changes in inspiratory muscle function. Patients in the IMT group exhibited significantly larger improvements in PImax in comparison to the control group (+29±15 vs. +1±12 cmH_2O, p<0.001). The IMT group completed 94±5% of sessions (based on data stored by the TFRL devices) and increased their training load from 45±2% to 81±4% of their baseline PImax (p<0.001).

The effects of adjunctive IMT on exercise capacity and dyspnoea sensation. A significantly larger increase in peak exercise cycle capacity was observed in the IMT group, which is consistent with a previous study [10]. Significantly higher levels of peak V_E (+3±6 vs. -2±7 L/min, p=0.013) and peak work rate (+13±14 vs. +2±12 Watts, p=0.004) were obtained in the IMT group, but dyspnoea intensity at peak exercise was not different between groups.

The effects of adjunctive IMT on breathing pattern at identical levels of ventilation (iso-V_E). At 80% and 100% of baseline V_{Emax}, significant differences in the interaction effects of group*ventilation were found between groups for both V_T and f_R, between post-intervention and baseline (p=0.047 and p=0.004, respectively) (Figure 1). However, the deeper and slower breathing pattern adopted only by participants in the TFRL-IMT group was not accompanied by changes in inspiratory flow rates. The V_T/Ti remained constant, with inspiratory (Ti) and expiratory (Te) time increasing proportionately, leaving duty cycle (Ti/Ttot) unchanged.

In the IMT group, there were significant correlations between changes in PImax and changes in breathing pattern (V_T (r=0.448, p=0.001), and f_R (r= -0.417, p=0.003)) at 80% of baseline V_{Emax}. This supports a possible causal link between inspiratory muscle weakness and breathing pattern. In contrast with Wanke et al. (1994) who observed changes in breathing pattern only at at peak exercise, we also observed changes in breathing pattern at iso-ventilation [10]. The larger improvements in breathing pattern that we found at iso-ventilation after IMT, did not however translate into larger improvements in breathing pattern at peak exercise. Improvements in peak exercise capacity were comparable between studies.

Our second hypothesis was that patients would be able to perform faster contractions with their inspiratory muscles during exercise; resulting in reductions in inspiratory time and leaving more time for expiration, which in turn might ameliorate DH. However, the previously observed increased capacity to perform fast contractions, [11] did not result in significant between-group changes in inspiratory flow rates during exercise. This is consistent with previous data from Petrovic et al [13], who reported a similarly small *within* group difference (5% as compared to 7% in our study) in V_T/T_I, which also did not result in a significant *between* group difference after 8 weeks of inspiratory flow resistive loading (IFRL) [13]. It is possible that longer training durations are needed to achieve significance. Another possibility might be that specific breathing retraining strategies, during exercise, in combination with IMT might be needed to teach patients how to use their increased capacity to perform faster inhalations during exercise. Collins et al. (2008) previously observed that the combination of ventilation-feedback (VF) and exercise training changed Ti/Ttot, decreased exercise-induced DH, and increased exercise tolerance [14].

Based on the observed differences in results and differences in training methods in our study in comparison with the studies of Wanke et al (1994) [10], and Petrovic et al (2012) [13], a prospective study would be worthwhile comparing the specific effects of each training method on exercise capacity and breathing pattern head-to-head. In contrast to Wanke et al. who used maximal isometric contractions at

RV and high intensity MTL training [10], both TFRL-IMT, and IFRL-IMT (used by us and by Petrovic and colleagues, respectively) allow end-inspiratory lung volume (EILV) to enter the IRV, and permit higher inspiratory flow rates (i.e. higher shortening velocities) at high training intensities (i.e. resistances >50%PImax) [11, 13]. According to muscle length (lung volume) and pressure-flow specificity of IMT, this should provide a training stimulus that is more specific to the operating range and the contraction pattern of the inspiratory muscles during exercise, since the largest improvements in function should occur at the volumes over which IMT is performed and larger increases in inspiratory flow are expected with high velocity training [12, 15].

The main limitation of this study is the study design. Since a historical group of patients who participated in an identical PR program served as control subjects, a prospective randomised controlled study design will be needed to corroborate our findings. It also remains uncertain whether our observed effects on breathing pattern occurred due to a reduction in mechanical restriction on V_T expansion (reaching higher EILV) or due to a reduction in DH (reducing EELV). However, it seems most likely that the higher V_T would be due to higher EILV, and not to a lowering EELV, because Ti increased in proportion to Te and Ti/Ttot remained unchanged; however, more elaborate measurement techniques will be required to evaluate the effects of IMT on operating lung volumes.

In conclusion, the addition of IMT to a PR program in COPD patients with inspiratory muscle weakness resulted in a deeper and slower breathing pattern during exercise. Patients could achieve significantly higher peak work rate and exercise ventilation without increasing dyspnea sensation. Our findings provide encouraging preliminary evidence supporting an additional benefit of adjunctive TFRL-IMT on exercise breathing pattern.

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Figure legends

Figure 1: Changes in tidal volume (V_T) and breathing frequency (f_R) at the comparable percentages of baseline V_{Emax} (40, 60, 80, 100 and peak ventilation) at baseline and after training in the IMT group (1A and 1B) and the control group (2A and 2B). * $p < 0.05$ (baseline vs week 8) based on post-hoc tests from mixed model analysis, values represented as mean±SEM.