

Respiratory physiotherapy can increase lower esophageal sphincter pressure in GERD patients

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KEYWORDS Inspiratory muscle training; Hypotensive lower esophageal sphincter; Gastroesophageal reflux symptoms; Threshold IMT	Summary <i>Background:</i> Inspiratory muscle training (IMT) has been shown to increase diaphragm thickness. We evaluated the effect of IMT on mid-respiratory pressure (MRP) in patients with gastroesophageal reflux disease (GERD) and hypotensive lower esophageal sphincter (LES), and compared the results with a sham group. <i>Methods:</i> Twenty consecutive patients (progressive loading group) and 9 controls (sham group) were included. All patients had end expiratory pressure (EEP) between 5 and 10 mmHg, underwent esophageal manometry and pulmonary function tests before and after 8 weeks of training, and used a threshold IMT twice daily. The threshold IMT was set at 30% of the maximal inspiratory pressure for the progressive loading group; while, the threshold for sham-treated patients was set at 7 cmH ₂ O for the whole period. <i>Results:</i> There was an increase in MRP in 15 (75%) patients in the progressive loading group, with an average gain of 46.6% ($p < 0.01$), and in six (66%) patients in the sham group with a mean increase of 26.2% ($p < 0.01$). However, there was no significant difference between the groups ($p = 0.507$). The EEP also increased compared with measurements before training ($p < 0.01$), but it did not differ between groups ($p = 0.727$). <i>Conclusion:</i> IMT increased LES pressure in patients with GERD, in both the treatment and sham groups, after an eight-week program. Although there was no statistically significant difference between groups, suggesting the pressure increase in LES occurs regardless of the resistance load of the threshold IMT. These findings need to be confirmed in further studies with a larger sample.
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Introduction

Gastroesophageal reflux results from failure of the barrier mechanism of the lower esophageal sphincter (LES), allowing the distal esophagus to be exposed to gastric juice.¹ This loss of barrier function has been considered largely from a structural perspective, with manometry frequently demonstrating a defective LES in patients with gastroesophageal reflux disease (GERD).^{2,3}

Some studies have shown that contraction of the crural diaphragm increases LES pressure.⁴ Structural measurements by ultrasonography and anthropometric calipers have documented that the diaphragm thickness increases when resistance is applied during weight training.⁵ Another study showed an 8–12% increase in diaphragm thickness during contraction after a 4-week program of inspiratory muscle training.⁶

The inspiratory muscles, including the diaphragm, are morphologically and functionally skeletal muscles and, therefore, should respond to training in the same way as any locomotor muscle if an appropriate physiological load is applied.⁵ Patients who have LES pressure lower than 5 mmHg before treatment commonly have an early return of GERD symptoms. However, when the LES pressure is below 13.2 mmHg, there is a delayed remission of symptoms.⁷

Van Nieuwenhoven et al. demonstrated that both the number and duration of reflux episodes are increased during periods of heavy physical exertion⁸; more recently, Ayazi et al. found that an increased thoraco-abdominal pressure gradient can be associated with abnormal esophageal acid exposure. The authors stated that this phenomenon may explain reflux associated with the increased ventilatory effort that occurs with exercise and in some patients with pulmonary disease.⁹

We hypothesized that patients who have LES pressure between 5 and 10 mmHg would benefit from inspiratory muscle training to increase diaphragm thickness and LES pressure. The purpose of our study was to determine the effect of progressive inspiratory muscle training on LES pressure in these patients with GERD and hypotensive LES, after eight weeks, and to compare them with the results of a sham group.

Methods

Subjects were selected among the patients referred to the esophagus and motility outpatient clinics at the University of Sao Paulo School of Medicine – Department of Gastroenterology (HCFMUSP), between February 2009 and July 2010. We enrolled 20 patients who were diagnosed with GERD, according to clinical endoscopic criteria and pH metric findings. An esophageal manometry test was performed on all patients and this demonstrated hypotensive LES values between 5 and 10 mmHg. The values were recorded as the highest pressure zone prior to the point of respiratory reversal. All patients had normal pulmonary function, as assessed by the standard pulmonary functional test.

The same inclusion criteria were used to select a group of 9 subjects for the sham group for inspiratory muscle training (IMT), since it is unknown how LES pressure would respond to respiratory physiotherapy. Subjects from the patient and sham groups were excluded from the study if they had any cardiopulmonary disease; mental disorder; diseases of the connective tissue; esophageal, gastric, or duodenal surgery; consumptive disease; were pregnant or breastfeeding; addicted to alcohol; or smokers. No patients with a hiatal hernia were included.

In the progressive loading group, the training intensity was set at 30% of each patient's initial maximal inspiratory pressure (PI_{max}), as recommended by Brunetto et al.¹⁰ Sham IMT was defined as using the same type of IMT device at an intensity of <8.3 cmH₂O for normocapnic individuals.¹¹ Each patient underwent inspiratory muscle training, pulmonary functional test, and esophageal manometry.

Inspiratory muscle training

Inspiratory muscle training was performed using a pressure threshold (Threshold IMT, Respironics, Cedar Grove, NJ) over a period of eight weeks. The training protocol for both groups consisted of 40 maximum inspirations from the residual volume, twice a day (morning and evening), 7 days a week. The inspiratory load was always set at 30% of the patient's PI_{max} for the progressive training group. The sham group performed the respiratory exercises under a constant inspiratory load of 7 cmH₂O – the minimum allowed for the device.

 PI_{max} was chosen as the index for inspiratory muscular strength, reflecting the strength generating capacity of respiratory muscles during breathing.⁵ The value was measured in accordance with the Brazilian Guidelines for Pulmonary Functional Tests (2002).⁶ Every fifteen days, all patients in both groups were required to visit the lab so the PI_{max} could be measured. In the patients of the progressive loading group, the inspiratory training load was adjusted at 30% of the new PI_{max} value. Patients were encouraged not to modify their daily routine during the period of training.

Pulmonary functional test

Total lung capacity and maximal flow volume loops were assessed prior to inspiratory muscle training to ensure there were no airway obstructions or ventilatory restrictions. The measurements of PI_{max} and maximal expiratory pressure (PE_{max}) were documented for comparison with values obtained after respiratory training with "threshold IMT" (Fig. 1). All the patients were evaluated by the same examiner using MedGraphics Elite.

Esophageal manometry

The esophageal manometry test (Alacer Biomedica[®]) was repeated after eight weeks of IMT to determine the LES pressures {end expiratory pressure (EEP) and mid-respiratory pressure (MRP)}, and to evaluate possible changes compared with the esophageal manometry test done prior to IMT (Figs. 2 and 3). The recording of the manometry results were computer based and performed by the same examiner — who did not know which patients were from the progressive loading or sham group — to



Figure 1 "Threshold inspiratory muscle trainer" (Respironics, Cedar Grove, NJ).

decrease inter-operator variability and for standardization of results.

Statistical analysis

A repeated-measures analysis of variance (ANOVA) was used to identify pre-training and post-training differences between and within groups for EEP, MRP, PI_{max} , and PE_{max} .

The mean age was compared between groups through the *t*-Student test and associations between gender and group by the accurate Fisher test. Differences were considered significant at p < 0.05. All statistical calculations were performed using SPSS, version 18.

Analysis for the Commission of Ethics of the HCFMUSP

The protocol of this research (0922/09) was reviewed and approved by the Human Research Board at the University of São Paulo School of Medicine — Department of Gastroenterology. All the patients were informed of the nature of the study and provided written informed consent prior to testing.

Results

Patients' characteristics are shown in Table 1. No differences were detected between genders in the study (p = 0.237). The mean age of the patients was not significantly different between the progressive loading and sham groups (p = 0.774).

Pulmonary test of function

After an eight-week IMT program, an increase in PE_{max} was observed in 13 of 20 patients (65%) in the progressive training group, with an average increment of 29.1 cmH₂O (31.3%). There was an increase in PI_{max} in 16 patients (80%), with an average addition of 33.3 cmH₂O (40.0%). By the end of the eighth week, the PE_{max} varied from 93 to 177 cmH₂O, with an average of 135.8 cmH₂O, in the sham group. This represented a mean increase of 22.1 cmH₂O (19.5%). In 7 of the 9 controls (77%), there was an increase in PI_{max} , with an average gain of 19.0 cmH₂O (19.6%).

 PI_{max} was significantly increased after the eight-week IMT program (p = 0.0159). However, analysis of the interaction time/group showed that there was no difference in PI_{max} behavior between groups throughout time (p = 0.5157), since both had statistically significant increases in PI_{max} . After eight weeks of IMT, there were



Figure 2 Progressive loading group: lower esophageal sphincter before (left) and after (right) the eight-week program of inspiratory muscle training.



Figure 3 Sham group: lower esophageal sphincter before (left) and after (right) the eight-week program of inspiratory muscle training.

statistically significant increases in PE_{max} in both groups (p = 0.035); although, the analysis of the interaction time/ group showed there was no statistically significant difference in the increase of PE_{max} between groups throughout time (p = 0.302).

Esophageal manometry

In the progressive training group, an increase of LES pressure by MRP was observed in 15 of 20 patients (75%), with an average gain of 4.9 mmHg (46.6%). In 12 of the 20 patients (60%), there was an increase in EEP, resulting in an average gain of 2.4 mmHg (34.8%). In the sham group, an increase in MRP was observed in 6 of 9 controls (66%), with an average increment of 2.9 mmHg (26.2%). The average gain in the final EEP was 1.1 mmHg (15%).

There was a statistically significant difference in the increase of MRP after the eight-week IMT program in both groups (p = 0.006). However, analysis of the interaction time/group throughout time did not show a statistically significant difference in MRP (p = 0.541) (Table 2). After eight weeks of IMT, EEP was significantly different in both groups (p = 0.041); although, no differences were detected when comparing the groups (p = 0.435) (Table 2).

Discussion

Gastroesophageal reflux disease is a common problem that is expensive to diagnose and treat.¹² Alternative methods

Table 1Patient's characteristics.								
	Number of	AGE (range years)	Gender					
	patients		Μ	F				
Progressive loading group	20	50.1 (28-70)	6	14				
Control group	9	51.3 (40-61)	5	4				
p	-	NS ^a	NS ^a					
M: male; F: female. ^a $p = NS$ (not significant).								

of treatment are being investigated to avoid long periods of drug treatment or surgical procedures.¹³ Other well controlled studies evaluating new therapeutic options, to be used either alone or in association with well-established methods of treatment for GERD, are necessary.

We showed in this study that constant or progressive inspiratory muscle training increases LES pressure after eight weeks in patients with hypotensive LES pressure and GERD, when compared to the LES pressure before treatment. The pressure threshold inspiratory muscle trainer is used in assessments of inspiratory muscular strength, and is non-invasive and easy to use.¹¹ Progressive threshold loading is commonly utilized to increase inspiratory muscle strength, without the need for a learning or familiarization period.¹⁴

In this series, the pulmonary test of function and esophageal manometry were performed to evaluate the behavior of the LES (for both methods: end expiratory pressure and mid-respiratory pressure) in 20 patients with GERD and hypotensive LES, after an eight-week program of inspiratory muscle training. A sham group was used because there is a lack of standard measurements of LES pressures after threshold inspiratory muscle training.

The inclusion and exclusion criteria were set to obtain a representative sample of patients with GERD and hypotensive LES. Patients with pulmonary symptoms of any etiology or illnesses that could make it difficult to execute the IMT, as well as those with structural changes, were excluded from this study.¹⁵ Patients with conditions that could present alterations in the amplitude of contraction in the esophageal body or in the LES pressure were also excluded.¹⁶

Currently, little is known about the effect of threshold inspiratory muscle training on increasing LES pressure. A 10% increase in the diaphragmatic thickness was recently reported as a result of four weeks of IMT.⁶ Thus, there is a relation between the diaphragm and LES. The objective of our study became whether this increase in diaphragmatic thickness would affect hypotensive LES.

The pulmonary function test was performed on the two homogeneous groups before training, to exclude subjects with obstruction or restriction of the airways. After this, the respiratory exercise with threshold was carried out to

	Progressive loading group		Control group		p
	Before	After	Before	After	
MRP (range mmHg)	10.5 (7.5–13.8)	15.4 (6-29.1)	11.4 (8.4–14.3)	14.3 (7–26.1)	0.006
EEP (range mmHg)	7.0 (5.2–9.8)	9.4 (3.6-18.1)	7.3 (5.2–9.4)	8.4 (6-14.6)	0.041
Increase LES pressure for MRP	4.9 (46.6%)		2.9 (26.2%)		NS ^a
Increase LES pressure for EEP	2.4 (34.8%)		1.1 (15%)		NS ^a
^a $p = NS$ (not significant).					

Table 2 Mid-respiratory pressure (MRP) and end expiratory pressure (EEP) variation in progressive loading and control group after eight-week program of inspiratory muscular training in the lower esophageal sphincter (LES) pressure.

evaluate the improvement in PI_{max} . PI_{max} was chosen as an index for the measurement of inspiratory muscle strength, since there is a high correlation between PI_{max} and diaphragmatic thickness.^{6,17} By the end of the eight-week IMT program, the measurements showed an average increase in PI_{max} of 40% in the progressive loading group, corresponding to literature data on healthy individuals.¹⁸

It was not the aim of our study to test the response of PE_{max} in these patients, since the threshold IMT did not offer resistance to air flow during expiration. However, a significant increase in PE_{max} was observed throughout the study period in both groups. This finding can be explained by the improvement in ventilatory muscular strength and resistance when keeping a controlled respiratory pattern.¹⁹ Moreover, these types of training not only increase PI_{max} but also increase the lung volume.²⁰

The positive response by the end of the treatment was similar in both the progressive loading and sham groups; however, the patients in the sham group had fewer complaints with regards to the execution of the exercises of respiratory training, such as thoraco-abdominal muscular pain and dizziness. The patients were well adapted to the exercises, and all of them completed the training program.

The length of the IMT program seemed adequate since a significant increase in the values of PI_{max} was observed in both groups. The increment of strength was more expressive in the first weeks of training, as the threshold loading became less substantial in the last month. This can be justified by the influence of the learning effect on the execution of the exercise in the initial weeks of training, beyond the first habitual week of adaptation. This learning capacity is attributed to an improvement achieved through sensory conditioning,¹⁴ responsible for the significant change in pressure in the eight-week period.

This study was the first to demonstrate the effect of IMT on LES pressure. A statistically significant increase in LES pressure was observed in both groups after eight weeks of IMT. Although, no statistically significant differences between groups were identified in the analysis of the interaction time/group from our results, which suggests that the pressure increase in LES occurs regardless of the resistance load of the threshold IMT. These findings need to be confirmed in further studies with larger samples.

Conclusions

This study on the influence of an eight-week program of inspiratory muscle training on hypotensive LES, in patients

with GERD, indicated there was a significant increase in LES pressure, using esophageal manometry, in the progressive loading and sham groups. Other studies are necessary to confirm these findings with larger samples of subjects to determine the clinical impact of this pressure increase, analyze if these pressures can be maintained, and to verify the applicability of this program in specific groups of patients, such as those with non acidic reflux, asthma, or high surgical risk.

Conflict of interest statement

None declared.

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