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MINIREVIEWS

Respiratory physiotherapy in gastroesophageal reflux disease: A review article

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Abstract

Gastroesophageal reflux disease (GERD) is a frequent disorder which is expensive to diagnose and treat. Initiating therapy with empiric trial of proton-pump inhibitor is a well established strategy; however, symptoms of GERD do often persist regardless of effective medication. Nowadays, increasing interest concerning the efficacy and safety of chronic acid suppression with proton-pump inhibitors (PPIs), prompts a consideration for GERD treatment strategies related to the basic physiology of the lower esophageal sphincter, including modulation of its tone and ending of spontaneous transient lower esophageal sphincter relaxation, which contributes to reflux. Together, the lower esophageal sphincter and the crural diaphragm represent the major antireflux barrier, protecting the esophagus from reflux of gastric content. In order to prevent the need for enduring PPIs therapy or surgical procedures, substitute therapeutics approaches are being researched. Recently, studies have focused on the response of the respiratory muscles to inspiratory muscle training. As a result, inspiratory muscle training has emerged as a potential alternative for treatment of gastroesophageal reflux. The present report reviews the physiologic factors contributing to GERD, and presents the newly developed therapies that can be applied either alone or in association with available efficient GERD therapy.

Key words: Gastroesophageal reflux disease; Lower esophageal sphincter; Inspiratory muscular training; Threshold

Core tip: Gastroesophageal reflux disease is a common gastrointestinal condition in the Western world, but remains challenging to treat. Acid suppression with proton-pump inhibitors substantially improves medical therapy, though it is not successful in all patients. Recently, some studies have shown that inspiratory muscle training increases lower esophageal sphincter pressure in patients with gastroesophageal reflux disease. However, other well-controlled studies are needed to establish if there is a substantial gain and maintenance in pressure, as well as clinical improvement, and to access the influence of inspiratory muscle training in particular group of individuals.

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INTRODUCTION

Gastroesophageal reflux disease (GERD) is characterized by troublesome symptoms and/or complications, such as heartburn and regurgitation, caused by the reflux of stomach contents. The condition is classified according to the Montreal Group's Classification[1,2], and represents one of the most common gastrointestinal disorders in the Western world, with a prevalence of 10%-20%[1,3]. A large proportion of the adult population experiences GERD at least once a month, and nearly 10% of patients are affected by symptoms weekly or daily[4], thus affecting their well-being and quality of life[1].

ANATOMIC STRUCTURE

GERD occurs from exposure of the distal esophagus to gastric juice due to failure of the lower esophageal sphincter (LES)[5]. This failure in patients with GERD has largely been considered from a structural perspective[6,7]. The LES is placed where the esophagus joins the top of the stomach; the upper portion is positioned in the diaphragmatic hiatus, and its bottom is intra-abdominal. The LES is retained within the abdominal cavity by the phrenoesophageal ligament, an elastic fascia which attaches the diaphragm to the esophagus, avoiding stomach contents going up into the esophagus. This ligament, the diaphragm, and the LES contribute to the maintenance of gastroesophageal competence[8] (Figure 1).

The LES concedes coordinated passage of food into the stomach and venting of gas after meals, and reflux of acidic liquid contents back up into the esophagus is a common event in healthy adults, happening mainly during episodes of transient lower esophageal sphincter relaxation (TLESR), defined as LES relaxation in the absence of a swallow. The frequency of TLESR is similar between healthy individuals and those with GERD, but the refluxate tends to be more acidic in GERD patients[8,10].

The LES is comprised of both intrinsic and extrinsic musculature. Endoscopic ultrasonography shows that the wall of the distal esophagus is thicker than the wall of the body of the esophagus, indicative of an intrinsic sphincter[11]. This intrinsic muscle is originated from a semicircular arrangement of esophageal smooth muscle. The extrinsic striated musculature is compounded of the crural diaphragm (CD), which involves the upper 2-4 cm of the LES and increases its tone in the course of inspiration. The highest radial pressures occur where the intrinsic and extrinsic fibers combine, normally at or near the diaphragm[8]. Together, the CD and the LES play an essential role protecting the esophagus from the acidic gastric content. Klein *et al*[12] described that subsequently removal of the LES, a pressure zone is identified as consequence of the CD contraction.

Vegesna *et al*[13] and McGray *et al*[14] demonstrated that the lower esophageal circular sphincter and CD are two distinct structural entities. Vegesna *et al*[13] performed a study using an endoscopic ultrasound/manometry catheter pulled through the proximal stomach and distal esophagus and found that in 10/20 subjects, the right CD was the first to compress the esophagus. In two subjects, the left CD was the first portion to compress the esophagus, and both the left and the right CD compressed the esophagus at the same location in eight subjects. The authors showed that three distinct anatomic structures, the clasp and sling muscle fibers, CD, and lower esophageal circular smooth muscle fibers combine to form the anti-reflux barrier of the proximal stomach and distal esophagus[13].

It is known that when the LES and the diaphragm are detached, more reflux occurs comparing to in reduced hernia state. This disconnection allows reduction of basal LES pressure due to deficit of the intra-abdominal segment[8], and results in isolation of the intrinsic and extrinsic sphincteric components. Reduced pressures, particularly those that are less than half of normal, can promote an early return of symptoms in patients being treated for GERD[15]. However if the intra-abdominal pressure is reduced > 70% of baseline, gastroesophageal reflux disappears, though no changes will be seen in the LES pressure if the abdominal pressure declines quickly, as in paracentesis in ascitic patients[16].

Kahrilas *et al*[17] found that the peak end-expiratory high pressure zone (HPZ) is 2 cm above the esophageal-cardiac junction, 1 cm above the squamocolumnar junction and 0.5 cm above the hiatus. The HPZ has two discrete segments in individuals with hiatus hernia, each proximal and distal to the squamocolumnar junction, attributable to the extrinsic compression within the hiatal canal. Inspiration and abdominal compression mostly augment the lower segment[17]. McCray *et al*[14] showed that it is possible to divide the HPZ into its two components (the intrinsic LES and the extrinsic CD) using simultaneous high-resolution endoluminal sonography and esophageal manometry. The HPZ was characterized as the CD distally, and as an overlap of CD and LES proximally. During end inspiration, the CD contributes to the initial distal rise in pressure at the HPZ. In all subjects, peak pressure of the HPZ corresponds to an overlap of the LES with the CD[14].

TREATMENT

Proton-pump inhibitors

Treatment of GERD is targeted on arising the pH of the stomach's contents, which has primarily been achieved since the 1990s with proton-pump inhibitors (PPIs)[18].

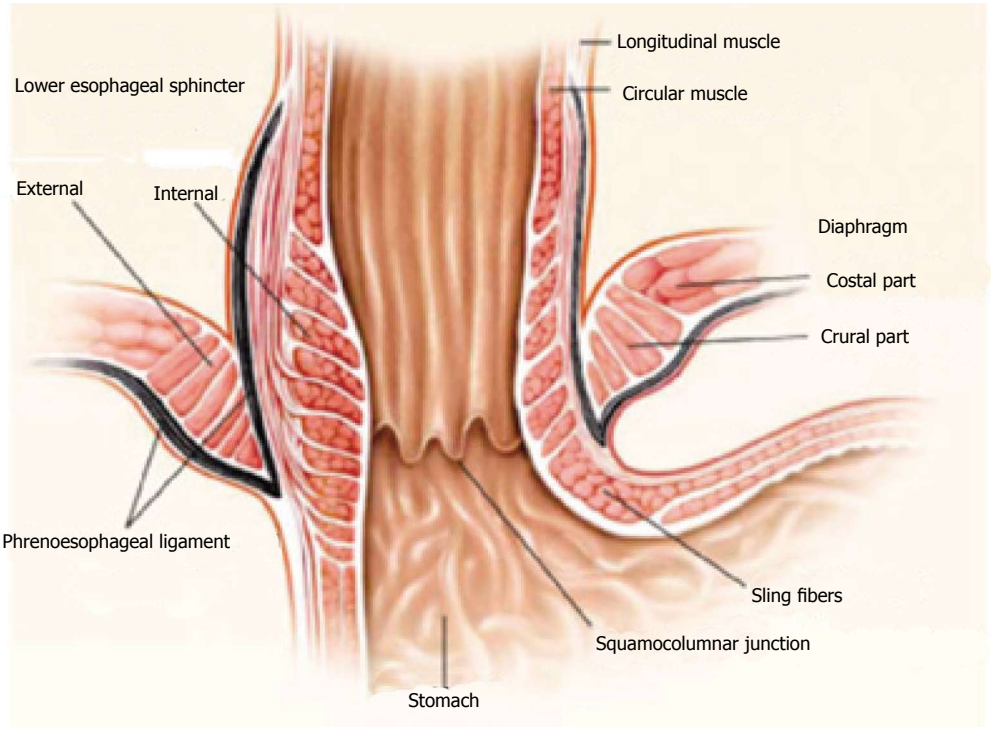

Figure 1 Sphincter mechanisms at the lower end of the esophagus[9]. This figure is reprinted with permission through the Massachusetts Medical Society, Copyright © 1997.

Currently, when a patient presents with symptoms typical of GERD, the initial pragmatic clinical strategy is two-month therapy with twice-daily PPIs. Once symptoms improve with therapy, patients should be stepped down to single-dose PPI[19,20]. For those whose ongoing symptoms are incompletely controlled with acid suppressants, an additional option is antacids, taken in response to symptoms, usually after meals[20], which act by locally raising the pH[21]. H2 receptor antagonists are reserved in general to control nocturnal acid breakthrough in spite of maximum PPI dose, or for maintenance treatment for GERD on an "as-needed" basis[12]. Nevertheless, treatment failures are inevitable regardless of which therapy is chosen[22].

The clinical effects of long-term maintenance treatment with PPIs have been a concern, including a raised liability of bone fracture, medication interactions, respiratory and enteric infections. Furthermore, once-daily PPI therapy fails to normalize esophageal acid exposure in a considerable percentage of adults who experiences reflux, particularly those with severe or complicated GERD. Patients with non-erosive reflux disease (the most common presentation of GERD), who account for the majority of refractory GERD patients, tend to continue to experience symptoms despite single-dose PPI therapy[8].

Refractory patients with documented data of continuing reflux as the cause of symptoms should be evaluated for further antireflux therapies. However, before moving to the next step, it is fundamental to identify lack of adherence among patients. In a cross-sectional and prospective study, 114/240 patients (47.5%) self-reported a low level of adherence to medication[23]. The factors identified with risk of non-adherence were age < 60 years, marital status, and being symptomatic.

Surgical procedures

Laparoscopic fundoplication substantially improves GERD symptoms, although symptoms return in some individuals, requiring the use of acid-suppressive medication[22,24]. In clinical trials, the risk of PPI use after antireflux surgery is 12%-44% within 1-2 years[25]. There are also some data to suggest that laparoscopic fundoplication is less effective at decreasing symptoms in partial responders to medical therapy than in complete responders[24,26]. Therefore, surgical therapy for GERD requires precisely indication and appropriate patient selection[19,23].

On the other hand, surgical invasiveness, cost, and inherent risks have created an interest in endoscopic therapies for GERD. Some of these endoscopic therapies include the Stretta radiofrequency procedure, in which radiofrequency energy is delivered through an endoscope to tighten the LES, the EndoLinch, in which an endoscopic sewing device is used[4], and the Enteryx, an endoscopic implantation of a bulking polymer into the muscle or deep submucosa of the LES[27]. The long-term efficacy, cost-effectiveness and impact of such procedures and risk for GERD-related complications have not been determined[26]. Currently, endoscopic treatment should be performed only in the

Table 1 Lifestyle modifications for treatment of gastroesophageal reflux disease[19]

Suggested	Uncertain
Treating obesity (reduce daily caloric intake, increase aerobic physical activity)	Reducing weight in patients with a normal body mass index
Changing alimentary habits (increase intake of fiber, fruits, and vegetables, and reduce intake of spicy and sweet foods and carbohydrate beverages)	Reducing acid beverage intake (orange or apple juice)
Reducing alcohol and coffee intake	Reducing tomato, tomato sauce, mint, and garlic intake
Elevating the head of the bed	
Avoiding strenuous exercises	

context of a clinical trial[27].

Lifestyle modifications

Lifestyle and dietary changes are considered the first-line treatment with the lowest possibility of side effects[16,19]. Treating obesity, stopping smoking, avoiding certain foods and alcohol, and elevating the head of the bed are recommended lifestyle adjustments for GERD. Nevertheless, few robust data have been published (Table 1)[19]. There is some physiologic evidence that exposure to tobacco, alcohol, chocolate, and high-fat meals decreases LES pressure. However, there is no evidence supporting an improvement in GERD measures after cessation of tobacco, alcohol, or other dietary interventions[28]. Observational studies of overweight and obese patients indicate that weight loss improves GERD symptoms, as obesity can alter esophagogastric joint (EGJ) anatomy and physiology by developing a significant spatial dissociation of the LES and the CD[19].

A national inquiry enrolling 13959 adults was conducted in 22 Brazilian cities. Individuals with GERD (defined as those with heartburn more than once a week) related their symptoms to food intake (55.0%), and fatty (25.9%) and spicy (11.7%) foods. Stress and health issues were associated to symptoms in 24.2 and 22.3%, respectively. In women, fatty foods prevailed, an expected finding as fat relaxes the LES and slows gastric emptying. Anxiety, tension, stress, and sadness were observed in 24.1% of GERD patients, once again with a marked prevalence of women[29].

Inspiratory muscle training

As morphologic and functional skeletal muscles, the diaphragm and other inspiratory muscles should react to exercise similarly to any locomotor muscle if a suitable physiologic load is administered. Indeed, structural measurements by ultrasonography and anthropometric calipers have also evidenced that after increasing loading exercise there was an improvement in diaphragmatic thickness[30].

The CD is an essential component of the esophago-gastric junction, the contraction of which can increase LES pressure[31]. CD function can be modified by inspiratory training[32], such as speech therapy and relaxation techniques, including diaphragm breathing exercises[19]. Da Silva *et al*[33] demonstrated a 9%-27% increase in LES pressure in patients who performed osteopathic manipulation techniques.

Initial studies by Carvalho de Miranda Chaves *et al*[34] indicated a positive result of inspiratory muscle training (IMT) on LES pressure. Using esophageal manometry they showed significantly higher LES pressure in adults with reflux after an eight-week IMT program; there was an increase in mid-respiratory pressure in 15/20 (75%) patients, with an average gain of 46.6%. The eight-week IMT program increased the maximal inspiratory pressure by 40%, as reported in previous studies[35]. Maximal inspiratory pressure is an index to calculate inspiratory muscle strength as it is highly correlated with diaphragmatic thickness[36,37]. Another study showed that four-week IMT results in a 10% gain in the diaphragmatic measurement during contraction[36].

The threshold IMT is utilized to evaluate inspiratory muscular strength. It an accessible, lightweight, portable and handy tool[38]. Progressive threshold loading is frequently applied to develop inspiratory muscle strength, without the necessity of special requirements or adaptation period[39]. As IMT has no recognized side effects, it would be appropriate for patients who commonly undergo extensive treatment[2].

In a randomized controlled study, Eherer *et al*[40] showed that actively training the CD as part of the LES using breathing exercises can diminish GERD as assessed by quality-of-life instrument, pH study, and on-demand PPI therapy. However, testing response of basal LES pressure augmentation post-treatment according to clinical improvement and patient well-being is mandatory, not only in patients with non-erosive GERD and healed esophagitis, but also in those with non-acidic reflux or extraesophageal symptoms[41].

A recent study evaluated the therapeutic mechanism of diaphragm training in 30 GERD patients using esophageal manometry with a Dentsleeve catheter and simultaneous esophageal pH monitoring, as well as ultrasonic imaging of proximal gastric volume[42]. The conclusion of the study was that diaphragm training the first hour after a meal might reduce postprandial esophageal acid exposure due to enhancement of antireflux barrier function by the EGJ. Therefore postprandial diaphragm training provides a new approach to conservative treatment of GERD. In

another research, IMT increased average EGJ pressure in GERD patients and reduced the number and duration of TLESRs[32], and thus may prove beneficial as a GERD add-on treatment.

CONCLUSION

Evidence-based reports concerning alternative GERD therapy are scarce. The fact that the LES together with the CD represent the major antireflux barrier, the response of the respiratory muscles to IMT has been an area of recent interest. IMT increases inspiratory muscle strength and diaphragm thickness. Rehabilitation therapy that acts on the CD is therefore a promising supplementary approach to treat reflux, decreasing the need for PPIs therapy or surgery. However, these findings have been based mainly on symptoms, and do not widely demonstrate a reduction of acid reflux events. Additionally, most studies have a small sample size and have been conducted for a short duration only. Quality of life scores, multichannel intraluminal impedance, and pH monitoring should be applied to these researches. As a result, further studies are necessary to ensure the clinical effect on pressure increment, whether these pressures can be sustained, and to validate the use of new methodologies in particular set of patients, such as those with non-acidic reflux, extraesophageal symptoms, or high-surgical risk.

Continual investigation of IMT will also elucidate the impact of various exercising protocols (frequency, intensity and duration of IMT, supervision) on results. Moreover, it is crucial to establish the extent to which changes in outcomes associated with IMT translate into clinically relevant progresses. We feel strongly that promising therapies will emerge in view of the large burden of GERD.

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