

Review Article

Management for Gastroesophageal Reflux Disease: Non-Medical Approaches

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Introduction

Gastroesophageal reflux disease (GERD) is a disorder in which gastric contents reflux recurrently into the esophagus, causing troublesome symptoms and/or complications [1]. The prevalence among western countries is quite high, ranging between 8.8% and 40% [2,3]. It also showed an increasing trend in Asia area [4]. GERD is associated with chronic cough, laryngitis and asthma [1] and it is believed that GERD patient are more likely to have obstructive sleep apnea [5]. In addition, overlap symptoms of GERD, functional dyspepsia and irritable bowel syndrome have been observed [6]. With the serious impact of quality of life, GERD caused a huge burden of illness, direct costs of \$4188 and indirect costs of \$8741 per patients annually [7].

Over the past several decades, the advancements in drug development have significantly improved disease management. Proton pump inhibitors (PPIs), due to their profound and consistent inhibitory effect on acid secretion, contribute a lot to the management of GERD and become the mainstay of treatments [8]. However, the efficacy is still not satisfied.

For example, about 10~15% of adult patients with erosive esophagitis fail to gain complete healing after 8 weeks of treatment [9]. Moreover, even when continuing the initial healing dose, there are still an approximately recurrence rate of 15~23% in patients with Los Angeles grades A and B, and 24~41% with grades C and D within 6 months. In addition, standard dose (once daily) PPI therapy is not beneficial to nearly 40% of non-erosive reflux disease (NERD) patients [10].

Besides, in spite of the conventional excellent consideration of the

Abstract

With the unsatisfied efficacy of drug treatment, non-medical treatments have been gaining an increasing attention through the past decades. Owing to the consensus of unhealthy lifestyles play an important role in the development and worsening of gastroesophageal reflux disease (GERD), lifestyle modifications come to the first line of disease management. Several interventions, such as evaluation of the head of bed, weight loss, smoking, certain food and drink cessation, have shown the beneficial effects for patients with GERD. Other non-medical therapeutics including anti-reflux surgery, breath training and acupuncture also have been proved to be efficacious. With a better understanding of these therapies, a better strategy would be recommended to achieve a superior management.

Keywords: Non-medical; Gastroesophageal reflux disease

safety profile of PPIs, a variety of side effects associating with long-term PPI use have been found recently.

Several population-based studies indicated that long-term PPI treatments were associated with community acquired pneumonia [11], Clostridium difficile colitis [12], microscopic colitis [13] and bacterial overgrowth [14]. Additional, an increasing risk of osteoporosis has been seen in the patients with long-term use of PPI [15]. It is likely that, PPIs reduce the gastric acid firstly. Then the calcium extraction from insoluble compounds, such as calcium phosphate or calcium carbonate, is disturbed [16]. Last, but not the least, the economic cost of PPI is quite high (approximately 10 billion in USA annually) [17]. Other drugs, such as histamine H₂ receptor antagonists and pro kinetics, are effective only in a subset of GERD patients, but the evidences are insufficient [8,15].

During the last decade, a marked decline has been seen in drug development, accompanying with a dramatic increase in testing of novel, nonmedical therapeutic techniques [18]. Several interventions, such as lifestyle modification, surgical treatments and alternative therapies, have shown the efficacies on treating GERD.

Lifestyle Modifications

Lifestyles have been paid an increasing attention with a great progress in the understanding of GERD. Weight gain [1], certain food intake [19], smoking [20] are believed to increase the risk of GERD. Moreover, it has been proofed that less adherence to guideline on lifestyle, including physical activity, sedentary habits, fruit consumption and processed meat consumption, was associated with the onset and evolution to esophageal adenocarcinoma in patients with Barrett's esophagus [21]. So lifestyle modifications are perceived

as the first-line therapy for patients with GERD [1].

Elevation of Head of the Bed (HOB)

The recommendation of HOB elevation to patient is on the ground of the theory that flat lying position is more likely to have gastroesophageal reflux events.

Significantly fewer reflux episodes, shorter reflux episodes, faster acid clearing, and fewer reflux symptoms were seen in GERD patients who slept with an elevated HOB (using 28cm blocks) compared with slept flat by pH monitoring [22]. A cross-over RCT of 15 GERD participants showed that elevation of HOB by a 10-inch wedge decreased the esophageal acid exposure (pH<4) compared with a flat position (15% and 21%, respectively; $P < .05$) and lead to shorter reflux periods and a rapid clearing of acid [23]. Recently, a self-control study demonstrated that a 6-days intervention of HOB elevation by 20-cm block could remarkably reduce the supine reflux time % (15.0 ± 8.4 to 13.7 ± 7.2 , $P=0.001$), acid clearance time (3.8 ± 2.0 to 3.0 ± 1.6 , $P=0.001$), number of refluxes 5 min longer (3.3 ± 2.2 to 1.0 ± 1.2 , $P=0.001$) and symptom score (2.3 ± 0.6 to 1.5 ± 0.6 , $P=0.04$) respectively [24].

Smoking

Tobacco consumption was closely related to reflux symptoms [25]. An increased risk of GERD symptoms was found in long-term smokers compared with short-term smokers (OR=1.7, 95%CI, 1.4-2.0; $P<0.01$) [26]. Besides, decreased lower esophageal sphincter pressure (LESP) and esophageal clearance capacity [27]. 24-h esophageal pH monitoring showed that the acid exposure of 14 smokers with GERD who abstained from smoking for 48 hours was significantly decreased from 11.1 to 7.35% ($P<0.007$) [28]. In addition, daily reflux episodes were significantly decreased by 1-day cessation of smoking, while the total esophageal acid exposure was not altered [29].

Obesity

The relationship between obesity and GERD has been wildly accepted. And the severity appears to correlate with an increase in BMI [30]. A beneficial effect of weight loss on GERD symptoms has been observed in patients with a BMI > 25kg/m² [31].

A randomized, double-blind, sham-controlled study documented that esophageal acid exposure was significantly reduced during weight loss induced by surgical procedure [32]. Weight loss induced by bariatric surgery also showed a therapeutic effect in patients with GERD symptoms [33]. A prospective cohort study, enrolling 332 patients with BMI of 25-39.9 kg/m², indicated that weight loss could decrease the overall prevalence of GERD (15% vs. 37%, $P<0.01$) and mean GERD symptom score (1.8 vs. 5.5, $P<0.01$). Moreover, 65% had complete remission and 15% had partial remission of reflux symptoms [34].

Certain Food Cessation

Alcohol intake not only could decrease esophageal pH, cause reflux symptoms in health subjects [35], but also was seen as an independent risk factor for symptomatic GERD [36,37]. There is also a common belief that some food may induce or exacerbate GERD symptoms.

The LEGEND [38] study, involving 12653 patients in Japan,

indicated that sweet foods, greasy foods, spicy foods, alcohol and coffee intake were associated with reflux symptoms. After cutting down sweet food, greasy food, spicy food, alcohol and coffee 50.8%, 59.1%, 45.9%, 54.7% and 43.5% patients reported improvements in reflux symptoms respectively. However, the conclusion of certain food or drink cessation is still controversial. One systematic review concluded that there was no evidence supporting the efficacy of cessation of alcohol, or other dietary interventions in the management of GERD [39].

Meal Timing

The timing of meals also plays an important role in relation to esophageal acid exposure. Early dinner consumption was helpful in the reduction of nocturnal gastric acidity [40], whereas, late evening meal intake was found to increase supine acid reflux, especially in patients who were over weighted, with erosive esophagitis, or hiatal hernia [41].

Prospective, cross sectional analytical, multicenter study, which involved 1875 patients, demonstrated that regular post dinner walk and >3 hour dinner-bed time interval could significantly reduce GERD related symptoms [42].

Anti-reflux Surgery

A Cochrane systematic review from four randomized clinical trials involving 1232 patients comparing PPIs with fundoplication found that reflux symptoms were better controlled after fundoplication, but surgical patients more often had dysphagia [43]. The recurrence rate ranged from 10% to 15% time dependently after fundoplication, while PPI appeared the same rates, from 7% to 16% [44-47].

In the measurement of esophageal acid exposure, surgery also showed a beneficial effect. One trial (n=217) monitored the mean time with esophageal pH<4 after 3-months treatment, showing a decline from 13% to 1% in surgical group and from 10% to 4% following drug treatment [48]. Additional, the mean acid reflux score declined from 43 to 9 in the surgical group and from 37 to 18 in the medical group (a score >14.7 indicates clinically significant reflux) [48]. In LOTUS study, after 6-months treatment, both surgery and medicine significantly reduce the acid exposure, but the surgical group showed a superior effect (from a median of 13.2% to 0.4% in the surgical group and from 7.4% to 4.9% in the medical group; $P=0.002$) [49]. Another randomized clinical trial completed a 3-years follow up. The results demonstrated the acid exposure declined from 10% to 2% in surgical group and from 10% to 4% in medical group comparing to the pre-treatment level. However, the fundoplication group complicated with 1.4 more heartburn-free days/week than the PPI group ($P=0.008$) [47].

Overall, the different interventions appear to share a similar relapse rate. Fundoplication seems to be slightly better than PPI in term of acidity control, but it carries a higher risk of development of dysphagia after treatment.

As to cost effectiveness, the results altered time dependently according to a systematic review [50]. Within one year period, drug treatment was more cost effectiveness than surgery, while in long term management fundoplication might be a better choice. Furthermore, surgeons' experience is crucial to the success [1]. Last but not the

least, it should be bear in mind that surgery is not helpful in reducing the risk of development of malignancy in Barrett's esophagus [51].

Abdominal Breathing Exercise

An impairment of the closing mechanism of the LES is considered to be the main pathogenesis of GERD. The surrounding crura of the LES, diaphragm, is believed to play an important role in the development of GERD [52]. As a striated muscle, the crura of the diaphragm could be trained by physical exercise. So a hypothesis came out: training of the diaphragm with a breathing exercise could decrease reflux and improve symptoms of GERD [53]. A prospective randomized controlled study showed that breathing training could significantly reduce the time with pH<4 (9.1 ± 1.3 vs. $4.7\pm 0.9\%$; $P<0.05$), improve the quality of life (QoL) score (13.4 ± 1.98 vs. 10.8 ± 1.86 ; $P<0.01$) after 4-weeks intervention. After a 9-months follow-up period, a significant decrease in QoL scores (15.1 ± 2.2 vs. 9.7 ± 1.6 , $P<0.05$) and PPI usage (98 ± 34 vs. 25 ± 12 mg/week, $P<0.05$) were found in these patients who continued breathing exercise, whereas patients who did not train had no long-term effect [53].

Acupuncture

As an alternative therapy, acupuncture or electroacupuncture has been globally accepted over the past decades and widely used for gastrointestinal disorders including GERD. In one clinical study, acupuncture significantly reduce the total times of reflux (92 ± 64 to 47 ± 32 , $P<0.01$) and time with pH<4 (18 ± 8 to 10 ± 8 , $P<0.01$) after 6-weeks treatment [54]. Another clinical study showed that adding acupuncture to standard PPI could significantly improve heartburn, acid regurgitation symptoms and QoL comparing with doubling the PPI dose in patients who failed to standard PPI [55]. The potential mechanisms might through increase the LES pressure [56], reduce the transient lower esophageal relaxations (TLESRs), regulate the acid secretion and esophageal hypersensitivity [57].

Conclusion

With the unsatisfied efficacies of drugs, non-medical therapeutic techniques for GERD have been developed quickly. Although the evidences of these treatments are generally not high, some of them, such as weight loss and evaluation of HOB, have been introduced into the guidelines [1,15]. With further deep researches, non-medical treatments for GERD will provide stronger evidences, as well as superior efficacies.

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