

## Chronic Asthma and Gastro-Esophageal Reflux Disease: The Treatment Plans

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### ABSTRACT

Gastro-esophageal reflux disease (GERD) regularly occurs when stomach acid moves up from the stomach into the esophagus. GERD might be associated with chronic asthma symptoms such as coughing and breathlessness. According to several studies on children and adults, GERD is proven to have a close relationship with asthma. Medication treatment via proton-pump inhibitors (PPIs), such as Omeprazole, H<sub>2</sub> receptor blockers (Ranitidine), and other antireflux medications, is appropriate for ameliorating GERD and asthma. Moreover, surgery is another useful approach to GERD and asthma treatment. In this regard, Nissen fundoplication (laparoscopic) is a principal surgery method. Medical and surgical antireflux therapies are recognized as effective methods in the treatment of GERD-associated asthma. Our review included studies that evaluated treatment of GERD-associated asthma. These studies accentuated the critical role of acid reflux suppression in relieving the patients suffering from a difficult to control asthma.

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### Introduction

Asthma is a chronic inflammatory airway disease which is caused by genetic and environmental factors such as allergens, air pollution and other environmental chemicals (2, 3). Common asthma symptoms are as follows: wheezing, coughing, chest tightness and shortness of breath (1). Furthermore, Gastro-esophageal reflux disease (GERD), rhinosinusitis, and obstructive sleep apnea are among the factors associated with asthma (4).

GERD is one of the most common illnesses of the gastrointestinal tract, which typically occurs when stomach acid moves up from the stomach into the esophagus (5). Abnormal relaxation of the lower esophageal sphincter is another significant factor leading to GERD (6).

GERD is known as a chronic disease requiring life-long treatment. Many people suffer from heartburn, regurgitation, or

dysphagia as a result of GERD (7). Proton-pump inhibitors (PPIs) such as Omeprazole, H<sub>2</sub> receptor blockers such as Ranitidine (8) are the conventional medications used in GERD treatment. In addition, surgery can be an efficient method for the treatment of severe GERD. Nissen fundoplication laparoscopic is one of the common surgical approaches in this regard (9, 10).

It is proposed that in GERD, a vagovagal reflex is initiated in the esophagus into the trachea either by gastric fluid or micro-aspiration of gastric content. The aforementioned processes can associate GERD with chronic respiratory symptoms (11, 12), or might induce coughing and breathlessness.

GERD is likely to give rise to asthma symptoms. Additionally, asthma might cause reflux to increase by building up pressure in the

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thorax during respiration (13, 14). Investigative tests are able to differentiate between bronchial asthma and asthma-like symptoms induced by GERD. While, GERD is likely to give rise to asthma symptoms, paradoxically, asthma might worsen the reflux by increasing the pressure in the thorax during respiration (13, 14). There are investigative tests to differentiate between bronchial asthma and asthma-like symptoms induced by GERD. Endoscopy and esophageal pH monitoring have indicated a high incidence of reflux in asthmatic patients (12, 15).

Our review included studies that evaluated treatment of GERD-associated asthma. Numerous studies on both children and adults confirmed the fact that GERD and asthma are interrelated.

To our best knowledge from publications after 2000 until now, in Pubmed search engine about GERD, asthma and treatment, more than 700 articles approximately 705 articles in Pubmed search engine cover GERD and asthma, proposing that surgical and medication treatment are the two tried-and-true methods of relieving asthma and GERD. These studies accentuated the critical role of acid reflux suppression in relieving the patients suffering from a difficult to control asthma.

## Medications

### 1. *Lansoprazole*

Lansoprazole is an acid suppressor used in a number of studies to improve GERD-associated asthma. For instance, in a study carried out to investigate the effects of Lansoprazole, all 30 patients received Lansoprazole 30 mg for 8 weeks on a daily basis and consequently, symptom improvement during treatment was estimated. In over half of the studied patients (17 patients), a remarkable reduction in the severity of asthma as well as a change in the pulmonary symptom scores were observed (16).

In another study evaluating the effect of Lansoprazole, it was noted that many of the GERD symptoms were relieved after treatment. The airway hyper responsiveness was one of the symptoms that significantly ameliorated after the treatment by Lansoprazole 30 mg (n=6, p<0.03) in this study (17).

### 2. *Omeprazole*

Several studies have investigated the effect of Omeprazole on GERD and asthma. In a study by Kiljander et al., it was found that after 8 weeks of Omeprazole treatment, there was a considerable reduction in the nocturnal asthma symptoms whereas no significant improvement in terms of daytime asthma was witnessed in this study (18).

In another study regarding the same subject, Harding investigated 30 asthmatic

patients with GERD who had begun to take 20 mg/d of Omeprazole for 3 months. The results revealed that asthma symptoms and/or peak expiratory flow (PEFs) and pulmonary function improved by >20% and 73% in the patients, respectively (19).

A study by Meier was conducted to explore effect of Omeprazole (20 mg twice daily) on the pulmonary function of asthmatic patients with GERD. Meier and colleagues (20) studied the effect of Omeprazole (20 mg twice daily) on the pulmonary function of asthmatic patients with GERD. Four out of the 15 asthma patients (27%) who were studied showed some improvement in their pulmonary function (FEV1) after six weeks of treatment. The obtained results indicated that after receiving Omeprazole treatment, pulmonary function would also improve in some asthma patients who were also suffering from GERD (20).

Furthermore, Respirand et al. (21) observed that treatment with Omeprazole resulted in an immediate amelioration of the pulmonary condition, although other therapeutic measures, including high doses of Ranitidine, had failed (21).

Combination therapy with Omeprazole and domperidone in asthmatic adults with GERD was the main purpose of Sharma et al. In their study, quite in line with other studies, asthma symptoms decreased and pulmonary function improved (22).

In the year 2000, Alexander demonstrated that PPIs and/or antireflux surgery could contribute to the improvement of asthma symptoms in numerous patients while affecting the pulmonary function minimally (23).

### 3. *Cimetidine*

Cimetidine is one of the acid suppression medications used in a number of studies with regards to treatment of asthma and GERD. In one study, twenty asthmatic patients with GERD were investigated and the reflux and nocturnal asthmatic symptoms witnessed a remarkable improvement. Chest pain was also among the symptoms that was significantly alleviated during the cimetidine treatment in this study (24).

### 4. *Ranitidine*

In order to study the role of gastro-oesophageal reflux (GOR) as the cause of asthma, Gustafson et al. examined the effect of Ranitidine 300 mg, (150 mg if B.W. was less than 40 kg) as an inhibitor of gastric acid secretion on asthma over a period of four weeks. The obtained results were indicative of a significant reduction in nocturnal asthma symptoms in the patients with pathological GOR compared to normal GOR patients (25).

Moreover, Farcau et al. conducted a study to estimate the effect of antireflux therapy on asthmatic children. It was concluded that antireflux therapy could lead to a considerable improvement in some clinical and functional parameters in asthmatic children (26).

In another study, Ranitidine hydrochloride (150 mg, twice a day) was used in treatment; the results of this study revealed a prompt amelioration of the reflux symptoms and a less dramatic and more delayed improvement in the pulmonary symptoms. Moreover, the recovery of the esophageal erosions was made complete in most of the studied patients and a remarkable improvement in pulmonary function was observed as well (27).

### 5. Pantoprazole

Similar to Cimetidine, Pantoprazole is an acid suppression drug. This medication was used in some asthma and GERD treatment studies, one of which was conducted by Dos Santos et al. in 2007. In their study, patients with asthma and concomitant GERD were prescribed 40 mg/day of Pantoprazole for 12 consecutive weeks. The quality of life in these patients enhanced considerably after the treatment, while the symptoms of asthma significantly improved. However, the pulmonary function parameters did not show any significant changes (28).

### 6. Rabeprazole

Tsugeno investigated the use of Rabeprazole 20 mg on a daily basis for 8 weeks in asthmatic patients with GERD. According to his findings, PPI treatment resulted in relieving reflux symptoms and decreasing PEF in all the studied patients with GERD. Therefore, it is safe to say that treatment with Rabeprazole could be effective in the amelioration of asthma in non-steroid-dependent patients with symptomatic GERD (29).

### Surgical approach

Surgery is an alternative approach in GERD-associated asthma treatment and several studies have been done on this issue. In one of these studies, some patients with both GERD and asthma underwent reflux surgery. In study of Sontag et al. (2003), 62 patients enrolled including: 24 controls (antacids as needed); 22 medical (Ranitidine 150 mg t.i.d.); and 16 cases underwent surgical approach. The obtained results were indicative of a substantial reduction in asthma symptoms and overall clinical features, whereas the pulmonary function, pulmonary medication requirements, and survival changed minimally (30).

In another study, patients received cimetidine or underwent antireflux surgery within a six-

month period. In study of Larrain and colleagues (1991), patients divided to groups: Cimetidine, placebo group, antireflux surgery for a six-month period. In all studied groups, patients improved clinically showing a significant decrease in their pulmonary medication intake. In the long run, surgical group was able to maintain the achieved improvement (31).

Silva and colleagues used laparoscopic surgery in order to assess the symptoms of patients with GERD-associated asthma. They identified enrolled 30 patients with extra-esophageal symptoms related to asthma. The obtained results confirmed Laparoscopic Nissen Fundoplication to be effective in relieving the typical reflux disease symptoms as well as reducing the clinical manifestations of asthma (32).

In 2004, Kaufman et al. performed laparoscopic antireflux surgery (LARS) on a number of asthmatic patients. They observed that LARS was able to prevent reflux effectively, resulting in ultimate improvement of GERD-related airway symptoms in approximately 70% of the patients. According to their study, the improvement rate in GERD symptoms was approximately 90% (33).

The gastro esophageal junction (Stretta procedure) is a new GERD treatment method with minimal invasive effects. Through this method, low-level radio frequency (RF) energy is released (34-36) leading to an overall improvement in GERD symptoms, quality of life and esophageal acid exposure (37-40).

In another study, Liang and colleagues evaluated the Stretta RF treatment in GERD-related respiratory symptoms. The studied patients were followed up for 5 years. The findings of this study showed a significant reduction in symptoms, regurgitation, chest pain, cough and asthma scores (41).

### Conclusion

Medical antireflux therapy and surgery are effective methods in the treatment of GERD-associated asthma. For the purpose of medical therapy, PPIs, and H<sub>2</sub> receptor blockers are used. Lansoprazole, Omeprazole, Rabeprazole, Pantoprazole, Cimetidine and Ranitidine are also among the antireflux medications which were mentioned in the studied articles in the current review. Regarding the surgical approach, Nissen fundoplication laparoscopic is an example of conventional surgical methods for treatment of asthma and GERD patients. Finally, it seems that using PPI is a safe, simple and applicable approach in GERD-associated asthma treatment. However, further medical and surgical interventions may be required according to the situation of patient.

## Conflict of Interest

The authors declare no conflict of interest.

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