COPD and Gastroesophageal Reflux Disease: A Double Blow

Mradul K. Daga*, Lalit Kumar and Govind Mawari

Department of Medicine, Maulana Azad Medical College, University of Delhi, New Delhi-110002, India

Abstract: Chronic Obstructive Pulmonary Disease (COPD) is a chronic illness with a long clinical course characterised by episodes of worsening respiratory signs and symptoms due to acute exacerbations leading to increased usage of health care resources and much disability in later part of the life. Gastroesophageal reflux disease (GERD) is a common problem of the general population and has been seen by many researchers throughout the world as a potential risk factor for exacerbations in COPD due to micro aspiration of the gastric contents.

It is observed that the incidence of GERD in COPD is much more than its incidence in the general population. This may be due to gastroesophageal dysfunction, leading to decreased tone and pressure in the lower oesophageal sphincter and oesophageal dysmotility. Many medications used by patients with COPD or changes in respiratory mechanics with increased lung hyperinflation may lead to this gastroesophageal dysfunction. GERD is amenable to treatment by both medical and surgical methods. This should help in reducing the exacerbations and improving the quality of life in patients with COPD. Hence further studies are needed to understand the cause-effect relationship.

Keywords: Chronic illness, COPD, gastroesophageal dysfunction, GERD, LES, inflammatory response.

1. INTRODUCTION

COPD is a chronic illness with progressive course, in which there occurs an increased inflammatory response within the airways and airway narrowing which is not fully reversible [1]. Globally COPD is a major cause of significant morbidity and mortality, and its prevalence is increasing particularly in those aged 65 years and older [2]. It is now the one of the leading cause of death in the world. With the increase in research, it has been observed that COPD is not just limited to lung and there are many extrapulmonary manifestations and co morbidities that should be evaluated and treated. These co morbidities have the potential to complicate the clinical presentation of this condition. COPD has a long course which is frequently complicated by acute exacerbations [3]. These exacerbations lead to an increase in morbidity and mortality in such patients, along with poor quality of life [4].

GERD or heart burn is a common medical condition encountered by medical practitioners throughout the world which is characterised by the abnormal reflux of stomach contents into the oesophagus, oral cavity or even lungs leading to symptoms or mucosal damage or both [5, 6]. The prevalence of GERD varies throughout the world and it depends on the population studied, as well as its cultural and dietary habits. Its prevalence in the Western world is higher at 10-20% when compared to a prevalence of less than 5% in Asia [7]. GERD presents with wide range of symptoms which may be oesophageal like heartburn, epigastric pain, dyspepsia, nausea, bloating, and belching [8]. The extra oesophageal symptoms include chronic cough, asthma, laryngitis and dental erosions [9]. These symptoms are typically present after intake of meals or in a lying down position and they get relieved by acid lowering agents [10]. Many patients of GERD are asymptomatic with features of mucosal damage on endoscopy only. GERD is associated with long-term complications and a poor health-related quality of life which leads to significant socioeconomic burden [11-13].

Prevalence of COPD related morbidity and mortality is increasing globally. There is an urgent need to develop strategies and newer treatment modalities to reduce its impact. The possible association between GERD and COPD is seen in many studies [14-17]. Proper management of GERD in COPD patients may decrease the frequency of acute exacerbations. However, more studies are needed in this field before definite conclusion can be drawn.

2. CAUSE EFFECT RELATIONSHIP BETWEEN COPD AND GERD

COPD and GERD augment each other. El-Serag and Sonnenberg concluded that in patients with COPD there was an increased risk of oesophageal problems when they were compared with controls (odds ratio [OR] 1.43, 95% confidence interval [CI] 1.33-1.53) [18]. Another longitudinal cohort study in which two groups of patients were studied one with
GERD without any previous history of COPD and other group of COPD without any evidence of GERD. The follow up was for 5 years. It concluded that in patients who had GERD, there was an increased incidence of COPD with risk ratio of 1.17. It also highlighted the fact that the incidence of GERD in patients who already had COPD was 14.9 per 1000 patients with a relative risk of 1.49 [19].

3. PREVALENCE OF GERD IN COPD

The prevalence of GERD in COPD patients is much more than the general population [20]. Self-reported questionnaires put up the prevalence of GERD in COPD patients to be around 17-54% [21-27]. The prevalence of pulmonary micro aspiration ranges from 19% to 78% when oesophageal pH monitoring was done [28-30]. Wide variation exists in the reported prevalence due to multiple factors like the criteria used to define GERD, method used or even history of any anti reflux medication. Even in symptomatic patients with COPD the prevalence of asymptomatic reflux is around 20-74% [31]. Few important studies done in this field are listed in Table I.

4. PATHOPHYSIOLOGY OF GERD

GERD is due to abnormal relaxation of the lower oesophageal sphincter (LES) or diminished basal LES pressure [32, 33]. Lifestyle factors like stress, sleeping in a supine position, consumption of a meal immediately before sleeping or consumption of food rich in fat (delayed gastric emptying) or foods that lower the LES pressure (chocolate, onion, garlic, caffeine, alcohol, tomato products, citrus, and carbonated beverages) may trigger symptoms [34].

GERD influences the clinical profile of COPD patients by two mechanisms i.e. pulmonary microaspiration and vagally mediated reflex bronchospasm of the airways [35]. During the microaspiration the reflux of the stomach contents enters the larynx and the trachea which leads to its irritation and produces a local inflammatory response leading to cough, dyspnoea and wheezing. The trachea and the oesophagus share the same autonomic innervations and hence irritation of the oesophagus in the form of esophagitis may lead to reflex bronchoconstriction and thereby leading to exacerbations and increased symptoms of COPD [36]. The oxygen desaturation at night has also been observed during episode of gastro oesophageal reflux.

5. WHY GERD IS PREVALENT IN PATIENTS OF COPD?

There are a number of possible explanations for the increased prevalence of GERD seen in patients of COPD. These are summarized below:

---

Table 1. Prevalence of GERD in lung disease.

<table>
<thead>
<tr>
<th>Name of the Study</th>
<th>Population Studied</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased gastro-oesophageal reflux disease in patients with severe COPD Casanova C. et al. [21]</td>
<td>42 Patients of COPD not on any anti reflux medication studied with single channel, 24 hour PH monitoring.</td>
<td>GERD prevalence in COPD: 62%.</td>
</tr>
<tr>
<td>Prevalence of gastroesophageal reflux in end-stage lung disease candidates for lung transplant. D’Ovidio F et al. [22]</td>
<td>21 Patients not on any anti reflux medication studied by dual channel, 24 hour PH monitoring.</td>
<td>Asymptomatic GERD prevalence was 52%.</td>
</tr>
<tr>
<td>The prevalence of distal and proximal gastroesophageal reflux in patients awaiting lung transplantation. Sweet MP et al. [23]</td>
<td>21 Patients were studied by 24 hour dual chambered pH monitoring.</td>
<td>GERD prevalence in COPD was 43%</td>
</tr>
<tr>
<td>Increased prevalence of gastroesophageal reflux symptoms in patients with COPD. Mokhlesi B et al. [24]</td>
<td>100 Patients were studied with modified mayo questionnaire.</td>
<td>GERD prevalence in COPD patients was 26%.</td>
</tr>
<tr>
<td>Impact of gastro-oesophageal reflux disease symptoms on COPD exacerbation. Terada K et al. [25]</td>
<td>82 Patients of COPD were studied and analysed as per FSSG and QUEST questionnaire.</td>
<td>GERD prevalence in COPD was 27% according to FSSG questionnaire And 24% as per QUEST questionnaire.</td>
</tr>
<tr>
<td>Prevalence of benign oesophageal disease in the Danish population with special reference to pulmonary disease. Anderson et al. [26]</td>
<td>264 Patients of COPD were studied with 12 hour esophageal pH monitoring.</td>
<td>GERD prevalence in COPD patients was 8% only.</td>
</tr>
<tr>
<td>Study of gastro-oesophageal reflux disease in patients with mild-to-moderate chronic obstructive pulmonary disease in India. Kamble et al. [27]</td>
<td>50 Patients of COPD were studied with dual channel 24 hours pH monitoring.</td>
<td>GERD prevalence in COPD patients was 78% in Indian population.</td>
</tr>
</tbody>
</table>
1. Effects of Nicotine-GERD tends to be more severe in patients with COPD who have high smoking index and its severity is related to the pack years which is an independent factor for severe GERD. Nicotine is associated with a reduction in LES tone as nicotine induces relaxation of circular muscle. Post smoking there is evidence of increased acid exposure in upright position, increased frequency of reflux events and prolonged acid clearance due to decreased salivation [37, 38]. Tobacco smoking also leads to cough which causes the diaphragm to contract forcing stomach contents upwards contributing to GERD. Nicotine and other contents in the smoke may itself act as irritants to cause esophageal inflammation. Nicotine also leads to delayed gastric emptying and this may increase the chances of GERD. There is evidence of decrease in oesophageal motility along with reduced pressure of both the upper as well as the lower oesophageal sphincter due to effects of nicotine in COPD patients [39, 40].

2. Swallowing Dysfunction: In patients with COPD there is always some swallowing dysfunction due to in-coordination between muscles of respiration and phase of respiration. This coordination is normally needed to prevent against microaspiration [45]. Abnormal swallowing reflex is associated with an increase in the annual exacerbation rate in patients with COPD which leads to further in-coordination in swallowing, thus leading to increased GERD [41-43].

3. Altered Mechanics of Breathing: Even the changes in mechanics of breathing in COPD patients lead to GERD. Due to severe hyperinflation of lungs more inspiratory effort is needed to inhale and hence increase in pressure gradient between thorax and abdomen leading to GERD [44-46].

4. Anxiety: There is increased anxiety which may further increase the symptoms of GERD due to increased production of acidic reflux due to sympathetic overactivity.

5. Medications: COPD patients use a large number of medications like beta agonist, corticosteroid, anticholinergics and theophylline that further increase the risk to develop the symptom complex of GERD [47]. These medications are known to decrease the lower oesophageal sphincter tone and also decrease the oesophageal motility. Patients with GERD may also need more bronchodilators use as GERD predisposes to acute exacerbations of COPD [48].

6. Age of Patient: COPD is a disease of the older population and risk of GERD in COPD patients increases with increasing age of the patient. Individuals with age more than 60 years are specially at increased risk of GERD [49, 50].

7. Obesity: Obesity and increased body mass index is a risk factor for GERD in COPD patients. A greater BMI may alter the contour of diaphragm and influences the work associated with breathing [51-53].

8. Associated co Morbidities: Patients with COPD which have other illness like cardiac problems and obstructive sleep apnea which, increases the intrathoracic pressure during the episodes of apnea, leading to increased transdiaphragmatic pressure. This increases the movements of contents of the stomach into the oesophagus and thus increasing the risk of GERD.

6. DIAGNOSTIC TOOLS FOR GERD IN COPD

The symptoms of GERD and COPD may have similar presentations in the same patient so it becomes important that one ask specific questions in the history like when the symptoms of GERD appear, awakening from sleep, decrease in symptoms of GERD with use of inhalers. Many questionnaires are also available. A trial of proton pump inhibitor therapy may be given if signs and symptoms are suggestive of GERD. A 24 hour oesophageal PH monitoring may also be done to confirm the diagnosis of GERD which is the gold standard [54, 55].

GERD and pulmonary microaspiration can be diagnosed using the proximal oesophageal PH monitoring or detection of pepsin in the pulmonary secretions [56-58]. Pepsin has been detected in the Broncho alveolar lavage (BAL) samples of patients of COPD and lung transplant patients. It is also present in the exhaled breath condensate in COPD patients [59]. Pepsin was detected in 33% of patients with COPD when their sputum samples were analysed [60].

7. IMPACT OF GERD IN COPD

The cost of annual medical care in 2461 patients with COPD was analyzed and it was found that patient with the COPD and GERD phenotype had an expenditure of 36793 us dollars which was much higher when compared with patients without GERD phenotype which amounted to 24722 us dollars i.e. 36% more [61].

It is known that GERD acts as a precipitating factor in acute exacerbations of COPD. This was confirmed by a systematic review and meta analyses of seven observational studies over varying durations of one to one and half year which concluded that GERD increased the risk of acute exacerbations of COPD [62]. Many recent studies have also confirmed the same fact of increased risk of exacerbations in patients with GERD. Patients who have frequent day as well as night symptoms of GERD, have increased rates of acute exacerbation. GERD acts as an independent factor for increased risk of exacerbations and COPD patients with GERD are increasingly recognized as a group of patients who have this phenotype which predisposes them to increased risk of acute exacerbation [42, 63-66]. It is important to recognize this as GERD can be controlled by treatment with life style changes as well as proton pump inhibitor therapy. This may potentially decrease the rates of acute exacerbations. GERD in such patients also leads to the perception of a poor quality of life by the patient and hence leading to further depression and decreased health related quality of life [61].

8. MANAGEMENT OF GERD: CAN IT DECREASE RISK OF ACUTE EXACERBATION IN COPD?

GERD is a disease which can be managed by three approaches first being the life style modification followed by medical treatment and finally few patients may benefit from
a surgical approach. The major lifestyle management approaches include regular exercise, weight loss, avoidance of abnormal semirecumbent posture during sleep and not to sleep in left lateral position and avoidance of taking meals that may aggravate the reflux by altering the tone of lower oesophageal sphincter. One should avoid late night meals. Stress reduction with yoga may be of some benefit. These are the first line of management of GERD and may apply to any patient with GERD.

Drug therapy of GERD includes antacids, histamine 2 receptor antagonists and the most recent advanced proton pump inhibitors. These drugs may be used as a single agent or multiple agents, depending on the severity of GERD. Many studies have been done in patients with COPD to study the efficacy of antireflux drugs in decreasing GERD and possibly reducing the frequency of acute exacerbations of COPD. The results of these studies give contradictory results with few showing reduced rate of exacerbations and few other no benefit of proton pump therapy. Few of these are listed below:

1. Sasaki et al. conducted a single blind randomized study which included 100 patients of COPD with associated GERD and patients were given proton pump inhibitor therapy for GERD. A 12 month follow up of same patients showed a decrease in the frequency of acute exacerbations and common cold [67].

2. Moklesi et al. studied 100 patients of COPD and GERD and they were subjected to either a proton pump inhibitor, H2 receptor antagonist or an antacid therapy. They reported decrease in symptoms like cough without change in spirometry parameters [17].

3. Similar results were also obtained by Eryusel et al. in their study of 30 patients of COPD with GERD phenotypes [68].

4. Baumelar et al. concluded that COPD patients receiving acid suppressive therapy had similar rates of acute exacerbations when compared to COPD patients who did not receive the same [69].

5. John G. Mastronarde et al. also noted the failure of proton pump inhibitor therapy to improve respiratory symptoms in patients with other obstructive airway disease like poorly controlled asthma [70].

Till now studies that report impact of proton pump therapy on the lung function test of patients are rare and none show an actual benefit on the lung function tests.

9. SURGICAL METHODS

Those patients who despite adequate medical management fail to respond and have a severe impact on quality of life due to GERD symptoms and acute exacerbation, are the ideal candidates of Surgical management, with a Nissen Fundoplication. Nissenfundoplication may lead to improved lung function in patients with COPD. Hartwig et al. studied 20 patients of COPD following bilateral lung transplantation and Nissen fundoplication and observed greater FEV1 at the end of 1 year in patients with this procedure [71].

Hoppo et al. also reported improved FEV1 and FVC in 11 patients who received pre transplants Nissenfundoplication [72].

Despite the above management strategies of GERD in COPD many patients may still remain symptomatic suggesting the need for further studies.

CONCLUSION

GERD and COPD are very common problems in the society and a patient who has COPD may show wide range of atypical symptoms of GERD. It is important to diagnose this phenotype of population that has both GERD and COPD, as one disease may increase the manifestation of the other illness. Increased risk of GERD and pulmonary micro aspiration is seen in COPD patients leading to acute exacerbations in COPD causing high economic burden. Treatment of GERD in such patients may be helpful in reducing this burden as it decreases the frequency of acute exacerbations. The common approaches for the management of GERD include lifestyle changes and drug therapy. Surgical approaches are reserved for patients with severe symptoms. However, there is lack of concrete evidence to suggest that GERD treatment will definitely eliminate exacerbation in COPD patients, still proper management of GERD in such patients is critically important for reducing increased health care expenditure and quality of life.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

COPD and Gastroesophageal Reflux Disease: A Double Blow

Current Respiratory Medicine Reviews, 2018, Vol. 14, No. 2 81


