



Exacerbation of Chronic Obstructive Pulmonary Disease and Clinical Implications

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Abstract

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide, resulting in a significant increase in economic and social burden. The natural course of COPD is disrupted by exacerbations with short- and long-term impacts on patients and healthcare systems. Evidence-based guidelines state that early detection and prompt treatment of exacerbations are essential to ensure optimal outcomes and reduce the burden of COPD. Several factors can identify populations at risk of exacerbations. Implementing preventive measures in at-risk patients is an important goal in the management of COPD.

Keywords: Bronchodilators; Chronic bronchitis, Chronic obstructive pulmonary disease

Introduction

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease characterized by persistent, usually progressive airflow caused by an increased chronic inflammatory response of the airways and lungs to harmful particles or gases [1]. COPD is a leading cause of morbidity and mortality worldwide, greatly increasing the economic and social burden. COPD prevalence, morbidity and mortality rates vary by country [2]. In the United States, approximately 24 million Americans have his COPD, which kills approximately 120,000 people each year and is now the third leading cause of death.

The natural history of COPD is punctuated by exacerbations that severely impact patients and healthcare systems. This review provides a brief overview of COPD exacerbations and their impact, outlining at-risk populations, etiology, and current management and prevention strategies.

The Global Chronic Obstructive Pulmonary Disease Initiative (GOLD) identifies COPD exacerbations in the natural history of a disease characterized by changes in baseline levels of dyspnea, cough, and sputum production in patients beyond normal daily activities [3]. Day-to-day changes occur abruptly and regular medications need to be changed. COPD exacerbations are placing a huge burden on healthcare systems around the world. They are a major cause of morbidity, mortality and disease. It also accounts for the majority of hospitalizations. Exacerbation services account for over 50% of the total cost of COPD [4]. For example, in the UK they are the leading cause of medical admissions, accounting for 15.9% of hospital admissions and costing the national health system more than £253 million annually [5]. COPD exacerbations have both short-term and long-term clinical consequences. The time course of symptom resolution during acute exacerbations was assessed in a study that showed that in 50% of outpatient-treated exacerbations, the patient recovered from baseline symptoms within her 7 days [6]. However, in his 14% of these events, patient symptoms did not return to baseline 35 days after onset, and in some patients symptoms did not return to baseline.

Recurrent exacerbations are associated with the rapid decline in lung function that characterizes COPD. In one study, frequent exacerbating factors reduced forced expiratory volume in one second (FEV1) by 40.1 mL/year [95% confidence interval (CI) 38-42] vs 32.1

mL/year (95% CI 31-33) [7]. Recently, a 3-year longitudinal cohort study showed that exacerbations during the study were associated with excessive decline in lung function (FEV1), with an average decrease of 2 mL per exacerbation per year ($p < 0.001$) [8]. In addition, frequent exacerbations are associated with reduced physical activity, poor quality of life and even increased risk of death.

The 'exacerbation' phenotype of COPD was recently described using data from large COPD cohorts such as: B. COPD Genetic Studies and Studies "Evaluating COPD Longitudinally to Identify Predictive Surrogate Endpoints" (ECLIPSE). Hurst and his colleagues showed that COPD exacerbations were not random events but clustered in time such that there was a period of high risk of recurrent exacerbations within 8 weeks from the first exacerbation. . In addition, an analysis of exacerbations in 2,138 patients enrolled in the ECLIPSE study used spirometry measurements to define disease severity, with more frequent exacerbations (two or more) and have been shown to be more serious. Overall, 22% of stage II, 33% of stage III, and 47% of stage IV patients had frequent exacerbations during his first year of follow-up. In the same study, the single best predictor of exacerbation in all his GOLD stages was history of exacerbation. Other predictors were health status, presence of gastroesophageal reflux, and elevated white blood cells (WBC) [9]. Indeed, in a physician-consulting patient, dyspnea can be defined as chronic coughing and mucus discharge for her 2 consecutive years >3 months/year. This is associated with exacerbation and exacerbation of respiratory symptoms in COPD patients.

The goal of treatment for COPD exacerbations is to minimize the effects of current exacerbations and prevent subsequent progression of exacerbations. Depending on severity, exacerbations can be treated as an outpatient or inpatient. Outpatient treatment with pharmacological treatments such as bronchodilators, corticosteroids, and antibiotics is sufficient in most cases. Based on available evidence, early detection

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and aggressive prompt management of exacerbations are necessary to ensure optimal outcome. Unfortunately, many of her COPD patients do not report exacerbations to their doctors [10]. Therefore, it is imperative to educate patients about the signs and symptoms of exacerbations and develop a self-management plan that helps them seek advice early in an exacerbation.

Exacerbations of COPD have a significant impact on both clinical outcome and economic burden, so it is imperative that clinicians prevent these exacerbations from occurring. Current guidelines state that prevention of exacerbations is the primary goal of treatment [11]. Many modalities, both pharmacological and non-pharmacological, have been proposed to prevent exacerbations.

Smoking cessation is the intervention with the greatest potential to alter the natural course of COPD. Evaluation of smoking cessation factors in lung health studies shows that 25% of long-term abstinence rates can be achieved if effective resources and time are devoted to smoking cessation. A study of his 23,497 veterans in the United States showed that smoking cessation was associated with a reduced risk of his COPD exacerbation, with the magnitude of risk reduction associated with length of abstinence [12]. A systematic review of all the available literature supports the conclusion that even with severe his COPD, smoking cessation slows the accelerated decline in lung function and improves survival compared with continued smoking. doing. A recent study of the cost-effectiveness of smoking cessation programs showed that high-intensity smoking cessation programs had fewer mean exacerbations (0.38 vs. 0.60) and fewer hospital stays (0.39 vs. 1) per patient, and mean hospital stays. I was. Number of quitters at lower total cost (20 vs 9).

Vaccines

Several studies evaluated the use of influenza and pneumococcal vaccination, which are now routinely recommended for all patients with COPD of significant severity. One study that reviewed the outcome of influenza vaccination in a cohort of older patients with chronic lung disease demonstrated that influenza vaccination is associated with significant health benefits with fewer outpatient visits, fewer hospitalizations and reduced mortality.

A Cochrane database review of four studies in patients with COPD showed no evidence of efficacy for injectable antipneumococcal vaccines; however, in another study of the 23 serotype pneumococcal polysaccharide vaccine in patients with COPD, Alfageme and colleagues demonstrated that the vaccine was effective in the prevention of community-acquired pneumonia compared with placebo in patients younger than 65 years or those with severe airflow obstruction. However, no difference in mortality between the groups was seen [13]. Larger well designed studies are needed to examine the effects of pneumococcal vaccine in patients older than 65 years with COPD. Immunostimulants have also been reported to reduce the frequency of COPD exacerbations. A study of the immunostimulatory agent OM-85, a detoxified oral immunostimulatory bacterial extract, reported a reduction in exacerbations and serious complications of hospitalization in patients with COPD, and follow-up studies supported the use of this agent. Economic benefits have been confirmed. A recent randomized trial showed benefit, but patients were heterogeneous [14]. The drug is currently in use in Europe, but a systematic review of 13 studies involving 2066 patients found no consistent evidence of benefit. Further studies are needed to understand the mechanism of action of this immunostimulatory agent before defining its role in COPD.

Pulmonary Rehabilitation

The proof for the effectiveness of pulmonary rehabilitation may be very strong; however its effect on exacerbation charge is much less studied than different greater direct outcomes, which include exercising overall performance and fitness status [15]. Conducting such research now might be difficult, given the ethics of withholding rehabilitation for lengthy sufficient for an exacerbation to occur. Respiratory rehabilitation can also additionally enhance diagnosis in sufferers with COPD through addressing applicable danger elements for exacerbations, which include low exercising capacity, reduced tension and depression, imperative desensitization to dyspnea and discount in dynamic hyperinflation. The maximum convincing proof comes from the possible randomized manipulate trial performed a few years in the past in South Wales wherein sufferers who acquired pulmonary rehabilitation had on common 10.four days in clinic in comparison with 21.zero days in the ones randomized to get hold of traditional clinical treatment. Combined evaluation of effects from six trials together with 230 sufferers indicated that respiration rehabilitation decreased the danger of clinic admissions (pooled relative danger = zero.26) and mortality (pooled relative danger = zero.45) [16].

Disease Management Programs and Patient Education

Self-management interventions improve different outcomes in many chronic diseases. A study conducted in the COPD population found that establishing a simple disease management program, improving patient education about COPD exacerbation symptoms, and seeking help early reduced hospital admissions and emergency room visits and improved health care system outcomes. has been shown to reduce the cost of however, the above results suggested that implementation of home education and management programs for patients with COPD did not lead to a reduction in hospitalizations due to acute exacerbations of COPD [17], but rather an unexpected increase in all-cause mortality. Further research is needed to clarify the role of disease management and patient education in reducing COPD exacerbations.

Long-Acting Bronchodilators

Regarding long-acting muscarinic antagonists (LAMAs), the use of the long-acting anticholinergic tiotropium has shown significant efficacy in reducing COPD exacerbations [18]. The study "Understanding the Potential Long-Term Effects of Tiotropium on Function" (UPLIFT), which enrolled a total of 5,993 patients (2,987 in the tiotropium group, 3,006 in the placebo group), found that tiotropium was associated with a decrease in the mean number of showed that there is The associated rate of exacerbations was 14% ($p < 0.001$) at 4 years. The recently published POET-COPD Tiotropium Exacerbation Prevention Study was a 1-year, randomized, double-blind, double-dummy, parallel-group study to evaluate severe disease in patients with moderate or moderate-to-very severe COPD. and history of exacerbations within the past year [19]. This study showed that tiotropium was superior to salmeterol in prolonging the time to first exacerbation.

The role of other long-acting anticholinergics (some still in clinical development) such as acridinium bromide, glycopyrronium, and umeclidinium in preventing COPD exacerbations is poorly defined. Regarding LABAs, the use of salmeterol, formoterol, and indacaterol in COPD maintenance therapy has been shown to reduce COPD exacerbations. A recent meta-analysis reviewed 17 randomized trials to assess the effect of his LABA on COPD exacerbations. Salmeterol, formoterol, and indacaterol significantly reduced COPD

exacerbations compared to placebo. Salmeterol significantly reduced COPD exacerbations in both ICS-exposed and non-exposed groups. The pooled ORs were 0.79 (95% CI 0.67-0.92; $p < 0.01$) and 0.80 (95% CI 0.65-0.99; $p = 0.04$). Compared to twice-daily dosed LABAs, newer ultra-long-acting LABAs (ultra-LABAs) have been shown to improve efficacy and may provide improved compliance. Several new once-daily Ultra LABAs are in development [20]. The only Ultra-LABA currently approved is indacaterol. As more drugs in this class are developed and more safety and long-term data become available, their use in the treatment of COPD will increase.

There are several LABA/LAMA combinations under development for maintenance therapy in COPD, including indacaterol/glycopyrronium, formoterol/acridinium, vilanterol/umeclidinium, and olodaterol/tiotropium. The role of these agents in preventing COPD exacerbations is poorly defined and needs to be investigated.

Inhaled Corticosteroids

ICS consistently reduces exacerbation rates by approximately 25% and is recommended for this purpose in the GOLD guidelines. The European Inhaled Steroids in Obstructive Pulmonary Disease (ISOLDE) study evaluated the long-term effects of fluticasone on exacerbations in 751 of her COPD patients [21]. The median rate of exacerbations decreased by 25% from 1.32 per year with placebo to 0.99 with fluticasone propionate ($p = 0.026$). However, current guidelines do not recommend the use of ICS alone in COPD maintenance therapy, as their efficacy is significantly enhanced when combined with LABA.

ICS/LABA Combination

Results from the TORCH study showed that all active treatments were significantly superior to placebo in reducing the risk of moderate-to-severe exacerbations and exacerbations requiring systemic steroids (all $p < 0.05$). Combination therapy and salmeterol were also significantly superior to placebo in reducing the risk of exacerbations requiring hospitalization (both $p < 0.05$) [22].

Conclusion

COPD exacerbations are often caused by respiratory infections and are a significant cause of morbidity, disability, and mortality. One of the main goals of COPD management is to reduce the morbidity associated with exacerbations and improve the quality of life of patients with this disorder. Although many pharmacological and non-pharmacological interventions are available to prevent exacerbations, the extent to which such interventions reduce exacerbation frequency is still limited, so new interventions should be developed and appropriately designed.

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