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ORIGINAL RESEARCH

Gold Guidelines for COPD-An Update on COPD Management

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Abstract
The GOLD guidelines for COPD was initiated to achieve an effective pharmacotherapy,delay the progression of disease, prevent the occurrence of exacerbations and obtain a better patient outcome. It is updated on a regular basis and the recent edition has been published in 2021, which provides evidence-based recommendations from several healthcare bodies. Compared to the previous years, there are some changes in the GOLD report of 2021, however most of the features still remain the same. Assessment of COPD based on spirometry, presence of symptoms, risk of exacerbations, and presence of co-morbidities remains to be essential in the new report and long-acting bronchodilators continue to be the main mode of pharmacotherapy.Initial therapy should include both non-pharmacological and pharmacological approach and special importance is given to smoking cessation programmes. Pulmonary rehabilitation programme should be taken for maintaining a stable life style and special importance is given on vaccinations. Risk factors like inhalation of noxious particles, exposure to biomass fuel and smoking should be carefully identified and avoided as much as possible. Based on the current pandemic situation, a special chapter on COPD and COVID-19 has also been provided.

Keywords: COPD, GOLD guidelines, spirometry, smoking cessation, bronchodilators, corticosteroids, pulmonary rehabilitation, COVID-19.

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1 | INTRODUCTION

Chronic Obstructive Pulmonary disease (COPD) is a common, preventable and treatable disease, characterised by persistent respiratory symptoms and airflow limitation due to airway or alveolar abnormalities caused by various etiological factors like cigarette smoking and significant exposure to noxious particles or gases [1].Alpha-1 antitrypsin deficiency,structural changes of pulmonary artery, hyper-responsiveness of the airways and impaired lung growth in childhood are some of the host factors that are responsible for the development of COPD [2]. It is currently one of the top three causes of death in the world with about three million deaths annually.Globally, the COPD burden is projected to increase in coming decades because of continued exposure to risk factors and aging of the population.With increasing prevalence of smoking in the developing countries, and aging populations in high-income countries, the prevalence of COPD is expected to rise over the next 30 years [3,4].

The most common respiratory symptoms include dyspnea, cough and/or sputum production, that may be under-reported by patients. The pathophysiology is characterized by chronic inflammatory changes that lead to the narrowing of lungs and persistent airflow limitation [4].Various mediators like IL-6,8, Leukotrine-B4 and TNF-alpha are responsible for the inflammatory responses, the levels of which increase during an exacerbation.In some of the patients,chemokines and eotaxin underlie the eosinophil present in airway path. Reactive oxygen species may induce gene expression of many inflammatory mediators like TNF-alpha and IL-1.Thus,chronic inflammation and various inflammatory mediators impose pathological changes in lungs.Due to the inflammatory events, the amount of goblet cells increases, which triggers mucus secretion and causes impaired ciliary motility.Thickening of the smooth muscle and chronic injury in the airway tube leads to decreased forced expiratory volume (FEV1).In case of severe COPD, the purulence found and hyperinflation happens that leads to increased functional residual capacity (FRC).The increase in FRC limits the duration inhalation time and consequently causes dyspnea [5].

The two conditions that are mainly associated with it include chronic bronchitis and emphysema.Chronic bronchitis is a condition involving chronic or recurrent excessive mucus secretion into the bronchial tree with cough that is present on most days for at least three months of the year for at least two consecutive years in a patient in whom other causes of chronic cough have been excluded. It mainly involves increased mucus production, reduced mucociliary clearance, and gas exchange abnormalities. Persistent irritation of the airways lead to an exaggerated response and hypersecretion. Accumulation of mucus results in recurrent viral and bacterial infections and activation of macrophage and neutrophils which results in epithelial destruction, thickening of alveolar walls leading to blockage and destruction. Chronic bronchitis patients exhibit productive cough, dyspnea on exertion, prolonged hypoxemia, leading to cyanosis, and barrel chest. The patients are often regarded as “blue bloaters” for their appearance.

While, emphysema is defined as abnormal permanent enlargement of the airspaces distal to the terminal bronchioles which is accompanied by destruction of their walls yet without obvious fibrosis. It has a different etiology and can co-exist with bronchitis.There is a gradual and progressive loss of elastic tissues within the lungs due to an imbalance between proteolytic enzymes and protective factors. Under normal circumstances,Alpha-1 antitrypsin balances the proteolytic lysosomal enzymes but in COPD, either there is a deficiency or depletion, mainly due to smoking or genetic predisposition.As a result, there is a loss of elastic recoil in small airways and availability of gas exchange surfaces. Common symptoms include dyspnea even at rest, minimal cough,

Supplementary information The online version of this article (https://doi.org/10.52845/CMRO/2022/5-2-1) contains supplementary material, which is available to authorized users.

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scanty mucoid sputum, tachypnoea, and flushed appearance. The patients are often regarded as "pink puffers" for their appearance [6-8].

2 | METHODOLOGY

1.GOLD GUIDELINES

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines were first initiated in 1997 collaboration with the National Heart,Lung, and Blood Institute of Health, USA and the World Health Organisation (WHO).These guidelines had been initiated to achieve better patient outcomes and effective therapy. The first report of GOLD guidelines was published in 2001,after that in 2006 and again in 2011.Updates of the 2011 revised report were then released in January 2013, 2014, 2015, and 2016.Then the 2017 report was released, which was is the 4^{th} major revision of GOLD.The 2019 edition of GOLD report had been updated with important literature reviews of COPD research and care that was published from Jan 2017 to July 2018. The recent updates of GOLD guidelines were made in 2019, 2020, and 2021.Compared to the previous years, there are some changes in the GOLD report of 2021, however most of the features still remain the same [1,9].

2.KEY FEATURES OF THE GOLD REPORT 2021

2.1.Among the various etiological factors in 2021 GOLD guidelines, two key factors have been specifically stressed upon. Those factors include:

2.1.a. Genetic factor such as alpha-1 antitrypsin deficiency and overexpression of the gene encoding the enzyme matrix metalloprotease-12 (MMP-12) for its genetic polymorphism in European population has been identified to be more susceptible for the development of COPD [10-12].

2.1.b. Cooking with biomass fuel is a prognostic factor for COPD. Although there is some limited evidence about the usage of non-biomass fuel for cooking in order to reduce the risk of COPD.

2.1.c. Risk factors like inhalation of noxious particles, exposure to biomass fuel and smoking should be carefully identified and avoided as much as possible [13,14].

2.2. The GOLD report 2021, continues to recommend that diagnosis of COPD is based on the presence of symptoms and chronic airflow obstruction indicated by a post bronchodilator forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) ratio of less than 0.7 on spirometry [1,14].

2.3. Smoking cessation is an effective way to prevent the occurrence and exacerbations of COPD. If anyone is willing for smoking cessation, the strategy of 5A's (Ask, Advice, Assess, Assist, Arrange) could be utilised. Smoking ban in public places also increase the percentage of smoking cessation and reduces the harmful effects of passive smoking [15,16]

2.4. Centers for Disease control and Prevention (CDC)stresses upon the importance of immunisation in COPD and provides guideline to offer TdaP(Tetanus,Diphtheria, Pertussis) vaccine in patients with COPD who have not been vaccinated in adolescenceto protect against pertussis [17]

2.5. it has been recently found that methylxanthines when used alone show dose related toxic effect because of the narrow therapeutic window.It has great efficacy when used along with salmeterol [18, 19].

2.6. The GOLD report 2021, confirms the benefit of using a combination of long-acting beta-2 agonist (LABA) and long-acting muscarinic antagonist (LAMA) rather than monotherapy to reduce the risk of exacerbations [20].

2.7. Regarding the use of Inhaled Corticosteroids (ICS) there are two new guidelines.

2.7.a. A meta-analysis reveals that treatment alone with Inhaled Corticosteroid (ICS) have not significant benefit on mortality in COPD patient.

2.7.b. Studies have indicated that there is a lower incidence of lung cancer among the patients who have been treated with ICS especially in female subjects [21,22].

2.8. The updated report continues to recommend the use of blood eosinophil count as a marker to guide treatment choices to maximise benefit and minimise risk of using inhaled corticosteroid (ICS) therapy.

Clinical trials and observational studies have shown that higher blood eosinophil counts ($\geq$ 300) are predictive of the efficacy of ICS in reducing exacerbations whereas low counts are predictive of an increased risk of developing pneumonia [23,24,25].

2.9. Triple therapy (LABA+LAMA+ICS) is shown to be much more efficacious as compared to the fixed dose dual bronchodilator therapy in case of disease progression and mortality [26-29].

2.10. In case of mild exacerbations, erdosteine may have potential benefit. Studies have shown thatit effectively reduces the frequency of cough [30]

2.11. Randomized controlled trials suggest that there is no need to use beta blockers in COPD patient, not prone to cardiac complication [31,32].

2.12. High flow oxygen therapy (HFOT) is the main line of treatment in exacerbations.Exercise tolerance can intensify by this therapy.

2.13. A new report about high flow oxygen therapy suggests its use via high flow nasal cannula. This clinically improves respiratory failure condition [33].

2.14. According to various reports,non-invasive ventilation (NIV) reduces the morbidity and mortality in both hospitalized and post-hospitalised patients [34,35].

2.15. It is still being recognised that physical exercise and pulmonary rehabilitation improves lung function and reduces the prognosis of recurrent COPD.It includes exercise,self-management,patient education and behavioural changes [36].

2.16.For exacerbation cases, routine check-up should be prescribed to prevent further relapse.

2.17. There are some new guidelines given under the complications and co-morbidities of COPD like heart failure (HF), ischemic heart disease (IHD), gastroesophageal reflux disease (GERD), lung cancer. Any patient suffering from HF with COPD should be prescribed withbeta-1 blockers to reduce complication. However, it shouldn't be used in case of an acute exacerbation of COPD, as it may lead to an increased risk of IHD, cardiac myopathy, myocardial infarction and unstable angina [1,37]

2.18.The COVID-19 pandemic has posed a great challenge to the healthcare system worldwide in the pharmacotherapy of several diseases.The GOLD report 2021 takes this into consideration and provides some recommendations regarding the management of COVID-19 in COPD patients.

2.18.a.Swab test should be done if COPD patients show worsening of symptoms like breathlessness, fatigue, laziness etc.

2.18.b. Patients with COPD should follow basic infection control measures to prevent the development if COVID-19 infection. This includes COVID appropriate behaviour like social distancing, regularly washing hands, and wearing of masks [38].

2.18.c. The patient should not undertake spirometry unless the situation is urgent, like pre-surgery or any interventional procedures, and the medications prescribed to the patient during the pandemic should not be changed. If routine spirometry is not available, home measurement of peak expiratory flow (PEF) with validated patient questionnaires could be used to establish a possible diagnosis of COPD. However, it has a low specificity and does not correlate well with the results of spirometry [39,40].

2.18.d. The use of ICS in the treatment of COPD during COVID-19 pandemic is controversial due to the increased risk of pneumonia.However, it has an overall protective effect against exacerbations[41,42].

2.18.e. Hospitalised patients with COPD and moderate to severe COVID-19 and pneumonia should be treated with appropriate pharmacotherapeutic approaches, such as dexamethasone and anticoagulation to prevent venous thromboembolism. Management of acute respiratory failure should include oxygen supplementation, prone positioning, high-flow nasal oxygen, non-invasive ventilation, and invasive mechanical ventilation if indicated [43].

3 | CONCLUSION

The GOLD guidelines remain to be an important and unbiased guidance for all healthcare professionals in order to achieve better patient outcome in the management of COPD. It is being updated regularly based on the latest trends in COPD research and the latest edition was in 2021. However, there were no significant changes made to the recommendations on

the diagnosis, assessment and management of COPD and its exacerbations in the 2021 edition of GOLD report.Assessment of COPD based on spirometry, presence of symptoms, risk of exacerbations, and presence of co-morbidities remains to be essential in the new report and long-acting bronchodilators continue to be the main mode of pharmacotherapy.Initial therapy should include both non-pharmacological and pharmacological approach and special importance is given to smoking cessation programmes.The new recommendations also explain the importance of TdaP vaccination as a protective measure against pertussis. It is recommended that the use of ICS should be guided by the blood eosinophil count. Based on the current pandemic situation, a special chapter on COPD and COVID-19 has been provided which mainly suggests that the pharmacotherapy of stable COPD does not need to change during the coronavirus pandemic. In case of an exacerbation, or symptoms of COVID-19 they should be tested for SARS-CoV-2 infection and managed accordingly. Use of ICS in COVID-19 should be based on risk-benefit ratio and proper infection control measures should be followed to prevent spread of the virus.

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