Saudi COPD Group Newsletter

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VISION:

Prevention, earlier detection and providing the best medical care for patients with COPD will result in improved outcomes, quality of life and consequently a lower burden on the patients, their families, the healthcare system and the community.

MISSION:

To serve as a recognized group of excellence for a comprehensive, state of the art, evidence-based approach through providing scientific educational activities and research initiatives to healthcare professionals, patients with COPD and the general public.

BACKGROUND AND OBJECTIVES:

The Saudi COPD group is a scientific and educational group, working under the umbrella of the Saudi Thoracic Society (STS). The aim is to enhance awareness of COPD in healthcare professionals and increasing public health education regarding COPD for the patients and their families and in the community.

The objectives of the group will be achieved by organizing scientific educational activities, including conferences, seminars, courses and workshops for healthcare professionals and conducting public educational activities for the patients diagnosed with COPD in healthcare facilities or via social networks.

The group's members are physicians and others healthcare professionals with a deep interest and extensive experience in COPD diagnosis and management. They have a strong and continuous commitment to achieve the objectives of the group and improve the awareness of the disease and the quality of life of the patients with COPD.

The panel members of Saudi COPD group had selected the following recent papers from various journals related to all aspects of COPD hoping will be useful and helpful in your practice and patient care.

GOLD COPD DOCUMENT 2023: a brief update for practicing cardiologists

Abstract: Many patients seen by cardiologists suffer chronic obstructive pulmonary disease (COPD) in addition to their primary cardiovascular problem. Yet, quite often COPD has not been diagnosed and, consequently, patients have not been treated of their pulmonary disease. Recognizing and treating COPD in patients with CVDs is important because optimal treatment of the COPD carries important benefits on cardiovascular outcomes. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) publishes an annual report that serves as a clinical guideline for the diagnosis and management of COPD around the world and has very recently released the 2023 annual report. Here, we provide a summary of the GOLD 2023 recommendations that highlights those aspects of more interest for practicing cardiologists dealing with patients with CVD who may suffer COPD.

Reference:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10215047/

Abstract: Ensifentrine is a novel, potent, and selective dual inhibitor of phosphodiesterase (PDE)3 and PDE4 designed for delivery by inhalation that combines effects on airway inflammation, bronchodilation and ciliary function in bronchial epithelia. In Phase 2 studies in subjects with COPD, ensifentrine demonstrated clinically meaningful bronchodilation and improvements in symptoms and health-related quality of life when administered alone or in combination with current standard of care therapies. Ensifentrine is currently in late-stage clinical development for the maintenance treatment of patients with COPD. This review summarizes non-clinical data as well as Phase 1 and Phase 2 efficacy and safety results of nebulized ensifentrine relevant to the maintenance treatment of patients with COPD.

Reference:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10392818/

The efficacy of N-acetylcysteine in chronic obstructive pulmonary disease patients: a meta-analysis

Background: N-acetylcysteine (NAC) may reduce acute exacerbations of chronic obstructive pulmonary disease through an antioxidant effect. Due to the heterogeneity in studies, the currently available data do not confirm the efficacy of oral NAC therapy in chronic obstructive pulmonary disease patients. We hypothesize that chronic obstructive pulmonary disease patients receiving regular oral NAC therapy do not achieve improved clinical outcomes.

Objectives: The purpose of this meta-analysis was to determine the efficacy of long-term oral NAC therapy in chronic obstructive pulmonary disease patients.

Data sources and methods: The literature search was performed using the PubMed, Web of Science, and Cochrane Library databases to identify all included clinical studies. Studies were eligible for inclusion only if they directly compared the outcomes of NAC versus placebo in adults with chronic obstructive pulmonary disease between 1 January 2000 and 30 May 2022. All studies were included if they reported one or more of the following outcomes: number of patients with no acute exacerbations, forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), St George's Respiratory Questionnaire score, glutathione level, and adverse events.

Results: Nine randomized controlled trials were included in the meta-analysis. There were 1061 patients in the NAC group and 1076 patients in the placebo group. The current meta-analysis provides evidence that the number of patients with no acute exacerbations (965 patients receiving NAC therapy, 979 control group patients), change in FEV1 (433 patients receiving NAC therapy, 447 control group patients), change in FVC (177 patients receiving NAC therapy, 180 control group patients), change in St George's Respiratory Questionnaire score (128 patients receiving NAC therapy, 131 control group patients), change in glutathione levels (38 patients receiving NAC therapy, 40 control group patients), and adverse events (832 patients receiving NAC therapy, 846 control group patients) were not significantly different between the two groups.

Conclusion: NAC did not reduce the risk of acute exacerbation or ameliorate the decline in lung volume in chronic obstructive pulmonary disease patients.

Reference:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10026096/

Mucolytics for acute exacerbations of chronic obstructive pulmonary disease: a meta-analysis

Abstract: This meta-analysis explored the safety and effectiveness of mucolytics as an add-on treatment for chronic obstructive pulmonary disease (COPD) exacerbations. Based on a pre-registered protocol and following Cochrane methods, we systematically searched for relevant randomised or quasi-randomised controlled trials (RCTs). We used the Risk of Bias v2 tool for appraising the studies and performed random-effect meta-analyses when appropriate. We assessed certainty of evidence using GRADE. This meta-analysis included 24 RCTs involving 2192 patients with COPD exacerbations, entailing at least some concerns of methodological bias. We demonstrated with moderate certainty that mucolytics increase the rate of treatment success (relative risk 1.37, 95% CI 1.08-1.73, n=383), while they also exert benefits on overall symptom scores (standardised mean difference 0.86, 95% CI 0.63-1.09, n=316), presence of cough at follow-up (relative risk 1.93, 95% CI 1.15-3.23) and ease of expectoration (relative risk 2.94, 95% CI 1.68-5.12). Furthermore, low or very low certainty evidence suggests mucolytics may also reduce future risk of exacerbations and improve health-related quality of life, but do not impact on breathlessness, length of hospital stay, indication for higher level of care or serious adverse events. Overall, mucolytics could be considered for COPD exacerbation management. These findings should be validated in further, rigorous RCTs.

Reference:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9879332/

Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts

Background: In some patients with chronic obstructive pulmonary disease (COPD), type 2 inflammation may increase exacerbation risk and may be indicated by elevated blood eosinophil counts. Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin-4 and interleukin-13, key drivers of type 2 inflammation.

Methods: In a phase 3, double-blind, randomized trial, we assigned patients with COPD who had a blood eosinophil count of at least 300 per microliter and an elevated exacerbation risk despite the use of standard triple therapy to receive dupilumab (300 mg) or placebo subcutaneously once every 2 weeks. The primary end point was the annualized rate of moderate or severe exacerbations of COPD. Key secondary and other end points that were corrected for multiplicity were the change in the prebronchodilator forced expiratory volume in 1 second (FEV1) and in the scores on the St. George's Respiratory Questionnaire (SGRQ; range, 0 to 100, with lower scores indicating a better quality of life) and the Evaluating Respiratory Symptoms in COPD (E-RS-COPD; range, 0 to 40, with lower scores indicating less severe symptoms).

Results: A total of 939 patients underwent randomization: 468 to the dupilumab group and 471 to the placebo group. The annualized rate of moderate or severe exacerbations was 0.78 (95% confidence interval [CI], 0.64 to 0.93) with dupilumab and 1.10 (95% CI, 0.93 to 1.30) with placebo (rate ratio, 0.70; 95% CI, 0.58 to 0.86; P<0.001). The prebronchodilator FEV1 increased from baseline to week 12 by a least-squares (LS) mean of 160 ml (95% CI, 126 to 195) with dupilumab and 77 ml (95% CI, 42 to 112) with placebo (LS mean difference, 83 ml; 95% CI, 42 to 125; P<0.001), a difference that was sustained through week 52. At week 52, the SGRQ score had improved by an LS mean of -9.7 (95% CI, -11.3 to -8.1) with dupilumab and -6.4 (95% CI, -8.0 to -4.8) with placebo (LS mean difference, -3.4; 95% CI, -5.5 to -1.3; P = 0.002). The E-RS-COPD score at week 52 had improved by an LS mean of -2.7 (95% CI, -3.2 to -2.2) with dupilumab and -1.6 (95% CI, -2.1 to -1.1) with placebo (LS mean difference, -1.1; 95% CI, -1.8 to -0.4; P = 0.001). The numbers of patients with adverse events that led to discontinuation of dupilumab or placebo, serious adverse events, and adverse events that led to death were balanced in the two groups.

Conclusions: Among patients with COPD who had type 2 inflammation as indicated by elevated blood eosinophil counts, those who received dupilumab had fewer exacerbations, better lung function and quality of life, and less severe respiratory symptoms than those who received placebo.

Reference:

https://www.nejm.org/doi/10.1056/NEJMoa2303951?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

Introduction: Accumulated high-quality data from randomised controlled trials (RCTs) indicate that long-acting muscarinic antagonist (LAMA)/long-acting β2 agonist (LABA) combination therapy significantly improves clinical symptoms and health status in patients with chronic obstructive pulmonary disease (COPD) and reduces exacerbation risk. However, there is a growing concern that LAMA/LABA therapy may increase the risk of cardiovascular disease in patients with COPD. The aim of this paper is to determine whether the use of LAMA/LABA combination therapy modifies the risk of cardiovascular disease in patients with COPD.

Methods: Two reviewers independently searched Embase, PubMed and Cochrane Library to identify relevant RCTs of LAMA/LABA or LABA/LAMA/inhaled corticosteroids (ICS) for the management of patients with COPD that reported on cardiovascular end-points. The primary outcome was major adverse cardiovascular events (MACE), which was a composite of cardiovascular death, myocardial infarction or stroke.

Results: A total of 51 RCTs enrolling 91 021 subjects were analysed. Both dual LAMA/LABA (1.6% versus 1.3%; relative risk 1.42, 95% CI 1.11-1.81) and triple therapy (1.6% versus 1.4%; relative risk 1.29, 95% CI 1.03-1.61) significantly increased the risk of MACE compared with ICS/LABA. The excess risk was most evident in RCTs in which the average underlying baseline risk for MACE was >1% per year. Compared with LAMA only, LABA only or placebo, dual LAMA/LABA therapy did not significantly increase the risk of MACE, though these comparisons may have lacked sufficient statistical power.

Conclusion: Compared with ICS/LABA, dual LAMA/LABA or triple therapy increases cardiovascular risk in patients with COPD. This should be considered in the context of the incremental benefits of these therapies for symptoms and exacerbation rates in patients with COPD, especially in those with a MACE risk of >1% per year.

Reference:

https://erj.ersjournals.com/content/61/2/2200302.long

Abstract: Though it has been widely accepted that infections of the respiratory tract is associated with aetiology of acute exacerbation of chronic obstructive pulmonary disease (AECOPD), more recent techniques have shown emerging evidence on the importance of alterations of diversity and composition of microbiota itself in the disease process. Specifically, these alterations is widely present in COPD patients from a variety of populations, and is associated with severity of disease, frequency of acute exacerbation, as well as prediction of exacerbation. In addition, the microbiota from respiratory tract contributes to disease mechanisms, and more recently have been shown to interact with gut microbiota in a bidirectional way. Therefore, updating progress in the field is crucial as it not only reveals potential underlying mechanisms of the disease, but also highlights the potential utilisation of microbiota as a biomarker for disease prediction and as a target for treatment. In this narrative review, we summarize current updates on microbiota dysbiosis in COPD, including techniques for sampling and analysis of microbiota, recent findings on the presence of microbiota dysbiosis and its correlation with clinical prediction and prognosis of the disease, as well as its potential roles in disease mechanisms. In addition, how gut-lung axis contributes to COPD progression is also discussed. Finally, we addressed the utilisation of prebiotic and probiotic treatment for COPD. Together, we hope to provide useful information to advocate the use of microbial parameters as important tools for diagnosis, treatment and long-term follow-up for COPD patients.

Reference:

https://www.sciencedirect.com/science/article/pii/S0944501322002841?via%3Dihub

Readmission rate for acute exacerbation of chronic obstructive pulmonary disease: A systematic review and meta-analysis

Background: The readmission rate following hospitalization for chronic obstructive pulmonary disease (COPD) exacerbations is extremely high and has become a common and challenging clinical problem. This study aimed to systematically summarize COPD readmission rates for acute exacerbations and their underlying risk factors.

Methods: A comprehensive search was performed using PubMed, Embase, Cochrane Library, and Web of Science, published from database inception to April 2, 2022. Methodological quality was evaluated using the Newcastle-Ottawa Scale (NOS). We used a random-effects model or a fixed-effects model to estimate the pooled COPD readmission rate for acute exacerbations and underlying risk factors.

Results: A total of 46 studies were included, of which 24, 7, 17, 7, and 20 summarized the COPD readmission rates for acute exacerbations within 30, 60, 90, 180, and 365 days, respectively. The pooled 30-, 60-, 90-, 180-, and 365-day readmission rates were 11%, 17%, 17%, 30%, and 37%, respectively. The study design type, age stage, WHO region, and length of stay (LOS) were initially considered to be sources of heterogeneity. We also identified potential risk factors for COPD readmission, including male sex, number of hospitalizations in the previous year, LOS, and comorbidities such as heart failure, tumor or cancer, and diabetes, whereas obesity was a protective factor.

Conclusions: Patients with COPD had a high readmission rate for acute exacerbations, and potential risk factors were identified. Therefore, we should propose clinical interventions and adjust or targeted the control of avoidable risk factors to prevent and reduce the negative impact of COPD readmission.

Reference:

https://www.sciencedirect.com/science/article/pii/S0954611122003559?via%3Dihub