International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Pharmacological and Non-Pharmacological Management of Patient with Chronic Obstructive Pulmonary Disease: Literature Review

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Abstract:
Background: Long-term respiratory discomfort and restricted breathing are the hallmarks of chronic obstructive pulmonary disease, a lung condition that worsens over time. These abnormalities in the airways and alveoli are typically brought on by exposure to gas or other hazardous particles. Globally, the number of instances of COPD is rising daily, making it one of the diseases that causes morbidity and death.
Objective: To assess how COPD patients' quality of life, symptoms, and muscles are affected by a mix of pharmacological and physical therapy therapies.
Methods: According to the inclusion and exclusion criteria, fifteen papers were included for this review. The best outcome is achieved when pharmaceutical and therapeutic effects are combined.
Results: A combination of pharmaceutical and physical therapy interventions is necessary to lessen the effects of COPD, improve quality of life, reduce symptoms, and strengthen muscles.
Conclusion: The current study's literature evaluation found that improvements in pharmacological and physical therapy treatments successfully enhanced lung functioning in COPD patients. The bulk of research indicates that larger improvements in respiratory parameters were obtained when pharmaceutical and physiotherapy interventions were combined.

Keywords: COPD- Chronic Obstructive Pulmonary Disease, PR- Pulmonary Rehabilitation, IMT- Inspiratory Muscle Training, ICS- Inhaled Corticosteroids.

1. INTRODUCTION

An illness should only be defined in terms of the traits that set it apart from other diseases. Therefore, in contrast to earlier papers, GOLD 2023 provides a new definition of COPD that focuses solely on these traits, independent of its epidemiology, etiology, risk factors, and diagnostic criteria, each of which are considered independently. (1)

According to GOLD 2023, COPD is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, expectoration, and/or exacerbations) brought on by abnormalities of the airways (bronchitis, bronchiolitis), and/or alveoli (emphysema), which result in persistent, frequently progressive airflow obstruction. (1)

The respiratory rehabilitation (RR) program's value and contribution to reducing symptoms, enhancing quality of life, and addressing psychological issues are emphasized in the COPD management guidelines. This intervention should be viewed as a type of global health assessment that is followed by therapies tailored to the needs of the individual, such as exercise training, education, and behavioral therapy. (2)
As far as treatment plans go, RR is seen to be the most economical option. It is well established that people with COPD should undergo respiratory rehabilitation since it lowers hospital admissions and mortality among those who experience frequent exacerbations. A particular area of focus for RR is inspiratory muscle training (IMT). (2)
In cases of severe and very severe COPD, pulmonary rehabilitation (PR), which emphasizes aerobic exercise training, is suggested. It has been demonstrated that PR improves quality of life and exercise capacity. There has already been evidence that people with chronic respiratory failure (CRF) can benefit from PR in terms of exercise tolerance, dyspnea, and quality of life. However, it commonly happens that these individuals cannot maintain a workload that is high enough to fully benefit from the training program. (3)
High-flow nasal treatment (HFNT) is a new method that can be utilized to improve breathing while simultaneously supplying a wider range of oxygen concentrations. It can send warm, humidified air through a nasal cannula at a rate of up to 60 L/min, with or without supplementary oxygen. In the upper airways, HFNT can provide a positive pressure proportional to the set flow above a flow of 20 L/min. (3)

2. Pathogenesis of COPD

A significant pathogenetic component in COPD, oxidative stress plays a role in the emergence of a number of inflammatory disorders. Patients' lung cells are harmed when they are exposed to smoke or dust. High levels of reactive oxygen species (ROS) are produced by neutrophil buildup and excessive mucus secretion. RS causes the structure of lung tissue to be degraded and the oxidative inactivation of antiproteases to lose its inactivation. In addition of producing additional reactive oxygen species (ROS) and exacerbating the oxidative stress response, neutrophil aggregation also triggers the action of numerous inflammatory factors. Airway epithelial mucus is secreted by the oxidative system, and exposure to noxious gasses, like cigarettes, can induce oxidative stress, which leads to a significant build-up of reactive oxygen species (ROS) and controls the expression of genes related to mucus production. Moreover, mucus production is aided by epidermal growth factor synthesis. This type of factor frequently involves a signaling cascade that starts with the stimulation of airway cells by oxidants and ends with COPD. When it comes to the imbalance between protease and antiprotease that causes structural deterioration of lung tissue, the most important factor is the inactivation of α1-antitrypsin, which is the most active. Protease-antiprotease imbalance ultimately results from the high concentration of oxidants generated by noxious gases and oxidative stress, which also inactivates the antiprotease. (4)
Airway remodeling in COPD is facilitated by neutrophils and macrophages, which also have a major impact on the oxidative stress response in COPD. Under conditions of oxidative stress, neutrophils (which can secrete serine proteases such as matrix metalloproteinase (MMP) and neutrophil elastase (NE)) concentrate in huge numbers in the airways of people with COPD. In addition, MMP is much higher in emphysema patients. It passes through the lung's extracellular matrix, which is broken down by serine proteases, and causes the airway to remodel. The reaction to infection is sensed by neutrophils. When an infection stimulates neutrophils in patients with COPD, these cells will take up residence in the lungs, where they will phagocytose the infectious agent to produce bactericidal proteins and proteases. This

process also generates reactive oxygen species (ROS), which is the body's defense mechanism against oxidative stress and free radical damage. Increased pulmonary vascular permeability and worsening lung tissue deterioration can result from the inflammatory cytokine IL-6, which is generated by neutrophils and macrophages and can also cause the generation of elastase and oxygen radicals. (4)

Clinical guidelines have undergone significant revisions in recent years, mostly with reference to moderate to severe stages of COPD. This is because of the impact of significant trials like the IMPACT study and, more recently, the ETHOS trial. The results of these trials provided new information about the function of dual therapies, including LABA plus inhaled corticosteroids (ICS) or LABA plus long-acting muscarinic antagonist (LAMA) combination, as well as the function of LABA/LAMA/ICS triple-therapy in these patients. An important and revolutionary development in COPD research was that the IMPACT trial was the first to demonstrate a significant reduction of mortality risk as a hard endpoint. Furthermore, the criteria for selecting inhaled bronchodilators and inhaled corticosteroids (ICS) have also been made clearer by the findings obtained thus far. These criteria are based on the patient's profile and characteristics, including eosinophil levels and history of exacerbations. (5)

3. Methods

3.1. Eligibility

According to our criteria, 15 papers were found for this study, of which 9 were experimental investigations and 6 were literature reviews. Articles containing enough details about the effects of pharmacological and therapeutic interventions in COPD patients met the inclusion criteria. Articles that were published after 2005 and in the English language were included.

Science Direct, Google Scholar, PubMed, and other websites were searched for articles. Following were the search tactics applied to every database: "COPD" stands for "chronic obstructive pulmonary disease," and it is treated with medication and physical therapy. The independent factors in this study are pharmaceutical and therapeutic treatments, while COPD is the dependent variable.

The selection criterion is searching

Criterion	Inclusion	Exclusion
Language	English	Non- English
Timelines	2005- 2023	<2005
Literature Type	Journal (articles)	Conference
Publication	Final	In press

4. Literature Review

In this study, we attempted to evaluate the therapeutic and pharmacological effects on COPD patients. Airflow restriction caused by COPD is a disease state that isn't completely curable. According to **Daniels et al. (2017)**, the airflow restriction is typically progressive and associated with an aberrant inflammatory response of the lungs to toxic particles or gasses. The American Thoracic Society and The European Respiratory Society agree that COPD is characterized by a decreased maximum expiratory flow, a slow forced emptying of the lungs, a decreased expiratory time, and air trapping in the lungs. As a result, breathing becomes difficult during exercise and during daily activities **(de Araujo et al., 2015).** (6)

5. Pharmacological Treatment

Kaneski et al conducted a study in December (2021) In a clinical investigation in l-Menthol – a new treatment for breathlessness, the impact of l-menthol on the sensory-emotional features of laboratory-induced dyspnea in individuals with COPD was described. Investigations into its use in inspiratory muscle training and its outcomes when combined with exercise training are necessary.

Atukuri Dorababu et al conducted a study Recent Advances (2015–2020) in Drug Discovery for Attenuation of Pulmonary Fibrosis and COPD a few natural or biomolecule-based medications are effective against PF and have sufficient potential to be developed into promising PF inhibitors, according to research in this area. Comparably, CSe is a major risk factor for the development of COPD and can be one of many variables that induce COPD. COPD is another serious health concern for which medication research ought to be given top priority. This review includes brief summaries of recently published medications for COPD.

Nicola A. Hanania et al conducted a study on Treatments for COPD in which the complex and multifaceted character of chronic obstructive pulmonary disease (COPD) has made the development of effective treatments extremely difficult. To tackle this issue, pharmacological and non-pharmacological methods are combined; an outline of these methods and their potential future direction is provided. Treatment for COPD mostly consists of bronchodilators, which can be coupled with inhaled corticosteroids for increased effectiveness and reduced adverse effects. When more understanding is gained about the pathological mechanisms underlying COPD, a new generation of pharmacotherapeutic agents—most notably phosphodiesterase-4 inhibitors, which are already in the advanced stages of clinical development, and leukotriene B4 inhibitors, which are in the early stages of clinical development. Long-term oxygen therapy (LTOT), nasal positive pressure ventilation (nPPV), pulmonary rehabilitation, and lung-volume-reduction surgery (LVRS) are non-pharmacologic treatments for COPD. Since LTOT is the only treatment that has been demonstrated to alter survival rates in severe cases—aside from quitting smoking—its significance in COPD is well established. Although recent advancements are detailed below, the functions of nPPV and LVRS are less understood.

Frederico Leon Arrabal Fernandes et al conducted a study on Recommendations for the pharmacological treatment of COPD which is More and more people are responding well to COPD medication. Health care providers can offer customized and successful therapy through a variety of interventions, including behavioral modifications, lowering risk factor exposure, educating patients about the disease and its progression, oxygen therapy, rehabilitation, comorbidity management, surgical and pharmaceutical treatments, and end-of-life care. One of the main pillars of managing COPD is the use of pharmaceuticals, and substantial progress has been made in this field recently. It is getting harder and harder to understand the limitations, potential hazards, and advantages of any therapy method as medications and therapeutic combinations become more widely available. Twenty-four experts from around Brazil came together to create the current recommendations by critically assessing new data and organizing the key issues surrounding the pharmacological treatment of COPD. A graphic manual for COPD diagnosis and treatment was created, and it was modified to consider the local conditions in Brazil. Based on their applicability in clinical practice, ten questions were chosen. They discuss how each medicine or drug combination is classified, defined, treated, and what evidence is available. Each topic was addressed by two experts, and the responses were then combined in two stages: participant consensus and review.

For instance, when a smoker experiences symptoms or exacerbations, the gold standard in 2018 calls for

spirometry to be repeated once. If the results are positive, pharmaceutical treatment will begin; if the results are negative, the patient will need to reassess their symptoms. If the results are negative, chest CT and PFT completion may reveal both positive and negative diagnoses, such as emphysema or wall thickness. Finally, after three or six months, bronchodilator and assessment will begin.

Dave Singh conducted a study on Pharmacological treatment of stable Chronic obstructive pulmonary disease (COPD) is treated pharmacologically with the goal of reducing future risk factors for events including exacerbations, disease progression, and death. Variations exist in the way that COPD is heterogeneous, which influences how different medications work. To maximize therapy choices for every patient, COPD treatment has progressed toward a precision medicine strategy that integrates clinical and biomarker data. Blood eosinophil counts have been adopted as a biomarker for use in clinical practice due to the data supporting its use in predicting responses to inhaled corticosteroids (ICS) in patients with asthma. To create new double and triple inhaled combination treatments that contain ICS or long-acting bronchodilators, various groundbreaking randomized controlled trials have been conducted with COPD patients.

Rupert Jones et al conducted a study in 2011 was Optimizing pharmacological maintenance treatment for COPD in primary care which is the complex illness known as chronic obstructive pulmonary disease (COPD) is a major global cause of morbidity and mortality as well as a substantial financial and resource burden on the healthcare system. In primary care, COPD is still significantly underdiagnosed and undertreated, despite the availability of national and international recommendations as well as efficient, well-tolerated pharmaceutical medications. Since COPD is a preventable and treatable condition, primary care doctors and patients need to be made more aware of it. An increasing body of research indicates that early commencement of long-acting bronchodilator medication can greatly enhance the patient's quality of life (QoL) and long-term health. The long-term benefits of long-acting bronchodilators as maintenance treatment for COPD have been validated by recent large-scale trials. Numerous advantages have been demonstrated in some patient populations, such as enhanced QoL and lung function, decreased exacerbations, and, in certain cases, postponed disease progression and increased survival. This review examines recent advancements in our knowledge of COPD, including new and existing pharmacological treatment options. It also suggests actions to improve early diagnosis and pharmacological treatment of COPD in primary care settings.

Florence Schleich et al conducted a study in 2023 was Cytokine-targeted therapies for asthma and COPD which is Hyper eosinophilic severe asthma patients experience a 50% reduction in exacerbations when treated with anti-IL5 mepolizumab; hyper eosinophilic COPD patients only experience a 15% reduction in exacerbations. Efficacy was correlated with increased eosinophil counts upon admission, as observed in asthma investigations. These studies showed that mepolizumab markedly improved quality of life in severe eosinophilic asthma but not in COPD. By interfering with normal immunoregulation, environmental exposures can modify the microbiota and impact the emergence of sensitization.

Ariel A. Calderon et al carries out research in 2022 was Targeting interleukin-33 and thymic stromal lymphopoietin pathways for novel pulmonary therapeutics in asthma and COPD which is Alarmins such as interleukin-33 (IL-33) and thymic stromal lymphopoietin (TSLP) are released when airway epithelial damage occurs from insults like viruses and cigarette smoke. These alarmins are essential for the activation of immune cell populations like mast cells, eosinophils, and group 2 innate lymphoid cells. Although it was previously thought that both cytokines were largely responsible for type 2 (T2) inflammation, there is growing evidence that both alarmins also play a role in mediating non-T2 inflammation. This is

supported by data from recent clinical trials that included cohorts of patients with COPD and asthma who also had non-T2 inflammation. Asthma and COPD patients can now manage their symptoms with available treatments that also improve lung function and lower the frequency of exacerbations. Nevertheless, there is still a need for additional exacerbation prevention and lung function enhancement, especially for patients who are not responding to existing therapies. Exacerbations of moderate-to-severe asthma have been linked to epithelial cytokines/alarmins; biologics that target TSLP and IL-33, respectively, have been demonstrated to decrease exacerbations in both general populations and particular subsets.

6. Physiotherapeutic Treatment

Sara Lundell et al conducted a study in 2022 which is Participatory methods in a digital setting: experiences from the co-creation of an eHealth tool for people with chronic obstructive

Pulmonary disease, which is Understanding and incorporating end users' needs and circumstances, is crucial when involving them in the creation and design of eHealth using participatory techniques. The shift to digital communication platforms brought about by social distancing practices in recent times calls for a deeper knowledge of this context in participatory research. To design an eHealth tool for individuals with chronic obstructive pulmonary disease (COPD), the study set out to explain and assess a digital co-creation process. A convenience sample of seventeen individuals, comprising COPD patients, healthcare providers, family members, and a patient group representative, engaged in six internet workshops that facilitated co-creation under the guidance of Participatory Appreciative Action and Reflexion. Should it be required, user manuals, technical tools, and expert assistance were given. seminars with a variety of subject matter, pre-recorded videos, online lectures, and homework assignments to help participants advance their skills. A combination of member verification, questionnaires, and attendance tracking were used to evaluate the co-creation process's validity, experiences, and ownership. Depending on the situation, data analysis was done both quantitatively and qualitatively. Despite early obstacles from computer naivete and the usage of digital tools and platforms, experiences with digital co-creation were mostly favorable. There is strong evidence that a digital co-creation process is a workable approach due to the high levels of satisfaction, engagement, attendance rates, and agreement between individual and group viewpoints.

Michele Vitacca et al conducted a randomized controlled trial in 2019 which is Effect of high-flow nasal therapy during exercise training in COPD patients with chronic respiratory failure in Pulmonary rehabilitation (PR) is widely recognized for its beneficial effects in treating symptomatic chronic obstructive pulmonary disease (COPD). Most studies do not include advanced patients with chronic respiratory failure (CRF), who are typically unable to maintain a high enough workload to fully benefit from PR on exercise tolerance. On breathing patterns and ventilatory efficiency during exertion, recent research using heated and humidified high flow oxygen therapy (HFOT) demonstrated beneficial effects. Hence, we intend to examine the impact of utilizing HFOT against conventional oxygen administration via Venturi Mask (V-mask), at the same inspiratory oxygen fraction, on enhancing exercise endurance in COPD patients with CRF conducting a high-intensity exercise program. One hundred sixty-six COPD inpatients with CRF, selected from seven PR hospitals, will participate in this multicenter randomized controlled experiment. Two groups—V-mask versus HFOT—will be assigned at random to patients. Using whichever oxygen delivery equipment corresponds to their group assignment, all patients will engage in the same intense workout routine. At baseline, clinical and anthropometric information will be

gathered, including body mass index, diagnosis, spirometry, and comorbidities (using the Cumulative Rating Scale).

For instance, consider nasal high flow oxygen therapy for moderate obstructive sleep apnea, post-operative hypoxemia, acute exacerbation of COPD, procedural sedation, lowering CO2 levels, and pre-oxygenation before intubation.

Eva Vázquez-Gandullo et al was executed a study on Inspiratory Muscle Training in Patients with Chronic Obstructive Pulmonary Disease (COPD) as Part of a Respiratory Rehabilitation Program Implementation of Mechanical Devices which is systemic review Being a complicated and diverse illness with both pulmonary and extrapulmonary symptoms, chronic obstructive pulmonary disease (COPD) necessitates a patient-specific approach to care. National and international guidelines for the treatment of COPD have just been updated, and they emphasize the value of respiratory rehabilitation (RR) and how it can help patients with their symptoms, quality of life, and psychosocial well-being. In the realm of RR, inspiratory muscle training (IMT) has drawn particular attention due to its demonstrated advantages for patients with chronic cardiac disease, respiratory disorders, and dyspnea during exercise. IMT has also been shown to improve maximum inspiratory pressure, overall well-being, and health status. Non-pharmacological therapy approaches include respiratory rehabilitation, with IMT garnering attention as a component of the rehabilitation regimen in recent years. Developments in various mechanical devices that support programs under direct supervision and those under remote monitoring have favored the IMT. Certain devices, such as the AiroFit PROTM, PowerBreathe®, or FeelBreathe®, stand out among patients with chronic obstructive pulmonary disease and meet accessibility, ease of use, and positive outcome criteria. With its nasal design, which encourages more natural breathing, and its ability to be used in dynamic environments, this last gadget offers the added benefit of being able to be used while the patient exercises.

Jane Reardon et al conducted a study on Pulmonary rehabilitation for COPD in which Treatment for patients with chronic respiratory illnesses, most often chronic obstructive pulmonary disease (COPD), involves a comprehensive approach to their well-being, which is known as pulmonary rehabilitation. In the lifetime management of individuals with symptomatic chronic respiratory disease, pulmonary rehabilitation is thought to be crucial. An individualized rehabilitation program that incorporates many modalities, including advise on quitting smoking, fitness training, and patient self-management education, must be delivered with the optimal efficiency by a multidisciplinary healthcare team working in concert. Patients with chronic respiratory diseases have demonstrated improved health-related quality of life (HRQoL) with the help of fitness training and self-management education, which are essential elements of pulmonary rehabilitation.

Sanduni Madawala et al conducted a study on the primary care experience of adults with chronic obstructive pulmonary disease (COPD) patients report a variety of difficulties they encounter when dealing with medical professionals, some of which may be made worse by their refusal or incapacity to give up smoking. None, meanwhile, have thoroughly examined the primary care experiences of COPD patients in community healthcare environments. A range of 45 to 75 years old comprised the participants. Among them, two thirds were current smokers, and nine were female. Patients with COPD want their general practitioners to provide them with proactive and compassionate care. Negative care experiences were largely caused by stigma and fear of being judged, which made general practitioners' assistance less accessible when needed.

Cath O'Connor et al was conducted a study in 2018 which is inspiratory muscle training (IMT) an acceptable treatment option for people with chronic obstructive pulmonary disease (COPD) who have declined pulmonary rehabilitation (PR) and can IMT enhance PR uptake When it comes to patients who refuse PR, respiratory muscle training (IMT) can be a suitable option. This is especially true for individuals who have severe COPD or are afraid of experiencing dyspnea during exercise. IMT can be done at home while seated. Through inspiration against an externally targeted load, IMT increases the workload of the inspiratory muscles. A rise in maximal inspiratory pressure (PiMax) indicates that IMT has strengthened the inspiratory muscles, which is beneficial for those with COPD who frequently experience weakening in their respiratory muscles. IMT was determined to be suitable. When comparing PR to IMT, less obstacles in the form of opportunity, motivation, and capability were found. With the exception of one participant who withdrew due to severe arthritis, all participants were able to master the IMT abilities and were physically capable of using the device. IMT provides a spatial and temporal opportunity for physical and social use. As per the PR barriers, depression and anxiety were mentioned as contributing causes to dropout and non-compliance with IMT.

Danielle A. Baxter et al conducted a study in 2019 was Muscle energy technique for chronic obstructive pulmonary disease. The use of manual therapy approaches to address musculoskeletal problems may have a role in the management of COPD. Various outcomes have been observed in clinical investigations assessing the application of spinal manipulation, myofascial release techniques, soft tissue techniques, and osteopathic manipulative treatments to treat musculoskeletal issues in patients with COPD. Among these manual therapies, Muscle Energy Technique (MET) has been utilized to treat COPD. Osteopaths and physiotherapists are among the many manual therapy professionals who employ the gentle MET approach in their clinical practice. Treatment for hypertonic muscles and increased joint mobility are frequent uses for it. The range of motion in the shoulder joint, spine, and muscles may all be improved by MET. Nonetheless, it is believed to function by a complicated interaction of neurophysiological processes that affect tissue extensibility and tolerance due to pain regulation. It is believed that applying MET to the thoracic cage and related muscles may help improve the mechanical limitations frequently observed in COPD patients. This could have an additional impact on outcomes including dyspnea, ability to exercise, and pulmonary function. MET in enhancing health, dyspnea scores, and exercise ability.

7. Conclusion

The current study's literature evaluation found that improvements in pharmacological and physical therapy treatments successfully enhanced lung functioning in COPD patients. The bulk of research indicates that larger improvements in respiratory parameters were obtained when pharmaceutical and physiotherapy interventions were combined. As a result, this study confirmed the benefits of medication and physical therapy for COPD patients. Improvements in dyspnea, oxygen saturation, respiratory rate, forced vital capacity, forced inspiratory volume, forced expiratory volume in 1 second, functional capacity, and muscle strength and chest expansion are all demonstrated by these treatments. According to our research, these treatments are all beneficial for COPD.

8. Limitation

Notwithstanding these drawbacks, the research is the first known assessment of the literature assessing the benefits of pharmaceutical and physical therapy interventions for COPD. Some treatments are not covered in this study, thus more research is required.

Acknowledgement

I, Vaishali Saini, would like to express my gratitude Dr. Meena Gupta of the Amity University Department of Amity Institute of Health Allied Science for her unwavering support of my research and for spending a great deal of time reading my work numerous times. Her expertise and passion give me proper direction and much-needed inspiration.

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