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Diseases of the Respiratory Tract: Asthma and Chronic Obstructive Pulmonary Disease

Sara M Tony[1], Mohamed EA Abdelrahim[2]*

[1]Beni-Suef Specialized Hospital, Beni-Suef, Egypt

[2]Clinical Pharmacy Department, Faculty of Pharmacy, Beni-Suef University, Beni-Suef, Egypt

***Corresponding author:** Mohamed EA Abdelrahim, mohamedemam9@yahoo.com

Abstract: Short acting β_2-agonists (SABAs) such as salbutamol and terbutaline are commonly used in the treatment of asthma and chronic obstructive pulmonary disease (COPD). According to the guideline produced by the British Thoracic Society (BTS) and the Scottish Intercollegiate Guidelines Network (SIGN), SABAs are considered to be the first line of treatment in asthma management. The National Institute for Health and Clinical Excellence (NICE) guidelines also recommend the use of SABA as the first line of treatment for managing patients with COPD. The recommendations in NICE guidelines state that in COPD patients, breathlessness and exercise limitation should be first medicated with short-acting bronchodilators (including β2-agonists or anticholinergics) when it is required. Both salbutamol and terbutaline have been widely used for asthma and COPD, and they have been found to be extremely beneficial in the two pathologic conditions.

Keywords: Respiratory tract; Asthma; COPD

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1. Asthma

Asthma, also known as reversible airway obstruction, is defined as an increase in bronchial constriction as a result of exposure to various triggering factors that narrow the pulmonary airways and limit breathing capacity, followed by inflammatory changes. The symptoms of asthma include dyspnea, wheezing, cough, chest tightness, breathlessness, and poor exercise tolerance. Productive cough (produces sticky mucus) is also considered one of symptoms. The cause of asthma is still not well understood. Asthma, which is linked to the exposure to specific allergic (irritant) substances, such as pollen grains and dust mites, non-specific irritants, such as chemical allergic substances, or exercise is known as extrinsic or allergic asthma. In the absence of any possible external precipitating factors, asthma is referred to as intrinsic asthma. These triggers can lead to the release of chemical mediators, such as histamine and leukotrienes, from mast cells in an asthmatic's lungs. These chemical mediators give rise to bronchial lining irritations, bronchial narrowing, and also bronchial spasms. In severe cases, complete bronchial obstruction may occur, leading to the accumulation of carbon dioxide (CO2) inside the lungs, which can result in loss of consciousness or even death.

Unlike many other respiratory diseases, the symptoms are reversible either spontaneously (without intervention) or with medical therapy. The definite cause of asthma has not been identified. Also, there are no distinct pathological characteristics or diagnostic tests available for asthma. However, the three main characteristics of the disease are chronic inflammation in the pulmonary airways, airway hyperresponsiveness, and pulmonary airway obstruction.

Asthma is a form of hypersensitivity, in which the diameter of the bronchioles decreases due to constriction and inflammation occurring in the lining of the pulmonary airways. Inflammation takes place when the stimulated tissues become swollen and produce excessive mucus. This results in a medical condition known as bronchoconstriction (**Figure 1**) [1]. A partial or complete obstruction of pulmonary airways can give rise to an asthma exacerbation. In normal breathing, air is inhaled through the nose and mouth. It then descends to the trachea and passes through the pulmonary airways into the air sacs. During exhalation, air is expelled from the lungs in the reversed order. During an asthma exacerbation, the muscles that surround the airways contract to render the narrowing of airways. The airway lining swells as a result of inflammation and oedema (fluid retention), and with an increase in mucus secretion, the airways clog. In acute bronchospasm, it takes more effort to exhale than inhale; hence, more air is confined inside the air sacs at each breath. This phenomenon is known as the air-trapping phenomena. It requires urgent pharmacological intervention because an acute asthma exacerbation may even lead to death.

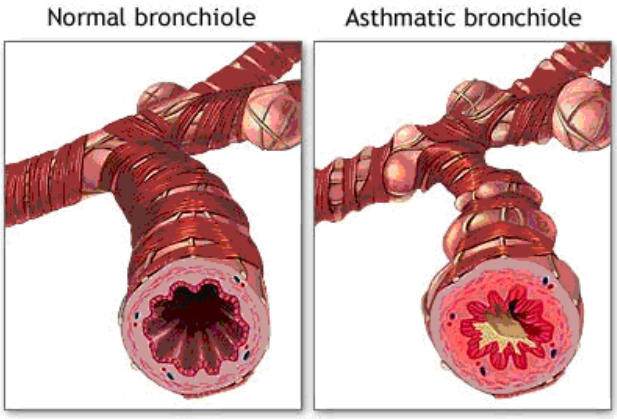

Figure 1. Bronchioles of a healthy individual and an asthmatic patient (reproduced from WebMD Medical Reference 2005)

The changes that occur in an asthmatic patient's lungs render the pulmonary airways sensitive to various triggering factors that do not usually affect the lungs in healthy non-asthmatic individuals. During asthmatic attacks, the muscles present in the walls of the bronchi contract, and the cells lining the airways become swollen and produce mucus, which accumulates in the air spaces.

Many asthmatic patients are sensitive to irritating foreign substances, such as pollen grains, house dust mites, and animal fur, which are known as allergens. Asthma can affect many patients who do not have allergies. Its symptoms differ from one patient to another. Some asthmatics may go for long periods without experiencing symptoms, only to develop sudden severe attacks for several days. The most common symptom observed by both chest physicians and asthmatic patients is wheezing. Wheezing is described as a whistling sound produced from a patient's chest during expiration. It may be very loud or just audible. Asthma can be classified into three categories: mild, moderate, and severe. This classification depends on the degree of pulmonary obstruction and its severity. Asthma often begins in childhood or adolescence, but it can occur even in adulthood. Although the symptoms of asthma in children and adults may be similar, there are some differences between the two. Children who have family history of allergies or asthma are more prone to be asthmatics later in life. Occupational asthma occurs when a worker is exposed to an

irritating substance that causes tracheal constriction. Brittle asthma refers to the transference of asthma from being well controlled to uncontrolled or poorly controlled within a short period of time.

During acute exacerbations, the rate of respiration increases, and tachycardia is commonly seen. Moreover, the peak expiratory flow (PEF) and forced expiratory volume in one second (FEV_1) are reduced to less than half (50%) of the predicted values. The main life-threatening signs include exhaustion, cyanosis (blue-colored skin), bradycardia, excessive decrease in blood pressure, confusion, and loss of consciousness.

2. Chronic obstructive pulmonary disease (COPD)

COPD is a major cause of morbidity and mortality all over the world, and it is the leading cause of death that is expected to increase in the coming years. Results from surveys have revealed that primary healthcare physicians tend to misdiagnose COPD with asthma and vice versa [2]. Chronic obstructive pulmonary disease (COPD) is distinguished by the obstruction of airflow. Airflow obstruction is known to be a progressive developing pathology, which is not completely reversible, and can last for several months without any notable improvement. The disease is mainly caused by smoking cigarettes [3,4]. Irreversible airflow limitation is considered to be the differential characteristic of COPD, and it can be measured during forced expiration [4]. Irreversible airflow limitation is caused by a delay in lung emptying as a result of either an increase in the resistance of tiny pulmonary airways [5], an increase in lung conforming due to lung destruction induced by emphysema [6], or both the causes together. COPD is characterized by a number of disease processes that result in pulmonary airflow obstruction due to the damage taking place in both the airways and lung tissues. Irritant factors, such as cigarette smoke, atmospheric pollutants, and infectious agents, can cause long-term inflammation of the bronchi [7]. This inflammation causes swelling of the bronchial mucous membranes, resulting in large amounts of mucous being secreted and its movement by cilia being hindered. When an irritant stimulates the bronchi for an extended period of time, the size of the bronchi shrinks and ventilation will be affected, resulting in bronchial inflammation (bronchitis). Emphysema also causes damage to the alveolar walls. The loss of alveolar walls reduces the surface area of the pulmonary membrane, thus reducing the lung capacity for gaseous exchange and exhalation. Both, bronchitis and emphysema can lead to COPD.

Figure 2 shows the data derived from a study carried out by Fletcher and Peto [8]. The results demonstrated the decreasing rates in FEV_1 with age for non-smokers and smokers who have or do not have COPD. The horizontal lines in the figure reflect the boundaries of COPD severity recommended by The Global Initiative for Chronic Obstructive Lung Disease (GOLD) [4]. The study showed that the decreasing rates in FEV_1 of most smokers are similar to those of non-smokers. The researchers also discovered that the lung function of a vulnerable fraction of smokers (about 15-20% of the total) rapidly deteriorated to levels consistent with moderate (GOLD 2), severe (GOLD 3), and very severe (GOLD 4) COPD. In addition, their findings revealed that stopping smoking has a beneficial effect on slowing down the rate of pulmonary deterioration at any age.

The figure depicts the rate of FEV_1 reduction in one smoker; however, other smokers will experience varying rates of decline, resulting in impairment at different ages [8] as lung inflammation affects those who smoke on a regular basis [9]. It is not known why only a small number of smokers show an extreme decline in FEV_1, but preliminary research results have revealed that the inflammatory response of lungs in the susceptible group appears to be enhanced [10]. According to NICE guidelines, smoking cessation should be the initial strategy for COPD patients, as long-term oxygen therapy can only enhance the survival period of patients with severe COPD (**Figure 2**) [11]. Pharmacological interventions attempt to alleviate symptoms and prevent exacerbations.

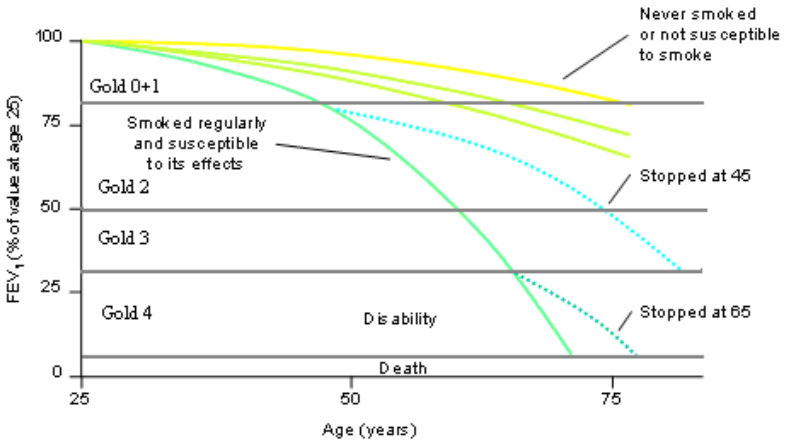

Figure 2. Natural history of COPD disease in patients of various ages

COPD is a slow-progressing disease that normally develops after a long period of smoking; however, other secondary risk factors can also play a role (**Table 1**). COPD is rare among non-smokers. Non-smokers who have COPD usually have alpha-1 antitrypsin deficiency.

Table 1. Risk factors associated with COPD

Risk factors
Exposure to tobacco smoke
Alpha-1 antitrypsin deficiency
Exposure to irritants at workplace, such as cadmium, silica, or dust
Low socioeconomic status
Vitamin C deficiency in diet
Pre-existing hyperresponsiveness of bronchial tubes
Low birth weight
Respiratory tract infections in children

However, some smokers are not liable to risk for unknown reasons. It could be related to an individual's genetic structure, which causes alpha-1 antitrypsin deficiency, resulting in low levels of protease inhibitors in smokers who have COPD (**Figure 3**) [12].

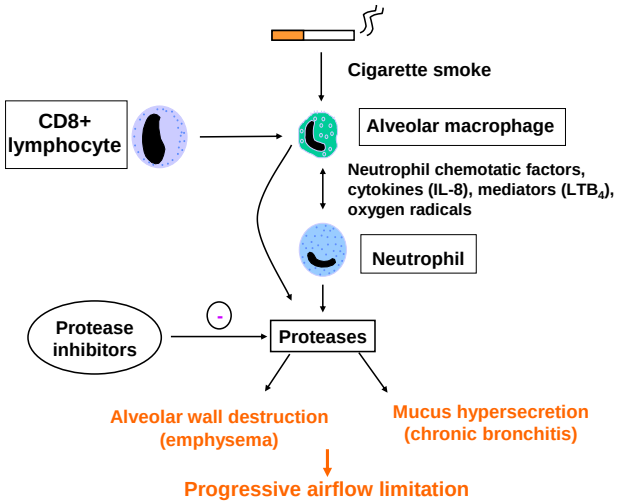

Figure 3. Pathophysiology of chronic obstructive pulmonary disease (COPD)

Over the last few years, there has been an alarming growth in the number of COPD patients admitted to hospitals. Hospitals are overburdened as a result of this (**Figure 4**).

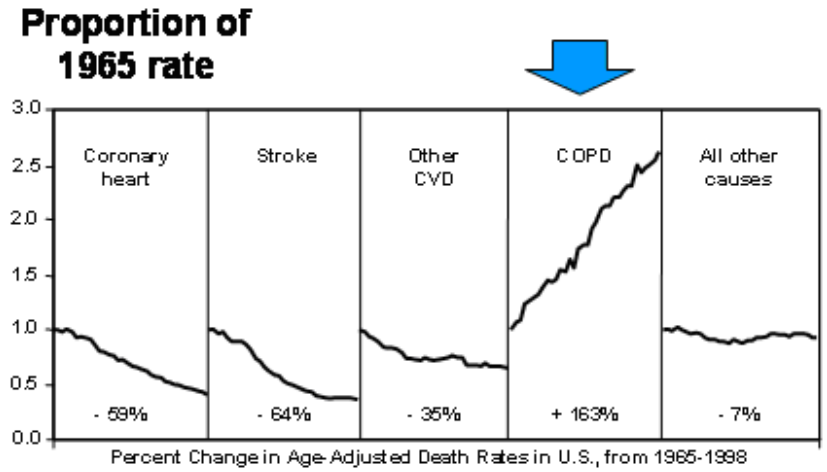

Figure 4. Increase in death rates of patients having chronic obstructive pulmonary disease (reproduced from Gold Guidelines)

3. Differences between COPD and asthma

(1) Although COPD and asthma share certain symptoms, such as coughing and wheezing, they are two distinct diseases in terms of etiology, onset, frequency of symptoms, and reversibility of airway obstruction. Asthma often develops during infancy or adolescence [1]. Smokers and former smokers in their mid-50s are more likely to acquire COPD [9,13].

(2) Irritants, cold air, physical activity, and infectious agents are the common causes of exacerbations in asthmatic patients, which are characterized by frequent wheezing, breathlessness, chest tightness, and coughing. On the other hand, exacerbations in patients with COPD are frequently triggered by pulmonary tract infections [1].

(3) The goal of treatment for asthmatic patients is to achieve near to normal lung function levels while also being symptom-free in between asthma exacerbations [1]. COPD patients usually experience symptoms almost every day. The airflow obstruction in COPD patients is not completely reversible unlike in asthmatic patients [3].

(4) In patients with COPD, their neutrophil count is higher compared to that in asthmatic patients. When compared to COPD patients, asthmatic patients have a higher percentage of eosinophils. Glucocorticoids are effective against eosinophil-mediated inflammation [14]; hence, these medications are effective in the treatment of asthma. Neutrophil-mediated inflammation is more resistant to treatment using glucocorticoids agents.

Quitting smoking slows the deterioration of lung function and reduces dyspnea, while the use of bronchodilators relieves symptoms [1]. Regardless of these distinctions, COPD is often wrongly diagnosed, and these patients are frequently treated as asthmatic patients [1]. In fact, a survey of 75 primary care physicians found that the same pharmacologic interventions are prescribed for both asthmatic and COPD patients [15].

For all asthmatic patients, the maintenance therapy consists of an inhaled corticosteroid (ICS) to control inflammation and a bronchodilator, which can be added as needed in order to relieve symptoms [1]. However, the opposite is true in the treatment of COPD. Bronchodilator agents are considered the first-line therapy for COPD. Treatment with ICS should be restricted to patients whose COPD is not well controlled with bronchodilators [1], as well as those who have moderate or severe COPD (FEV_1 50% predicted) and experience frequent attacks [3]. The differences between COPD and asthma are shown in **Table 2**.

Table 2. Differences in the diagnostic criteria between chronic obstructive pulmonary disease and asthma

	COPD	Asthma
Smoker or ex-smoker	Almost all	May be
Symptoms under age 45	Seldom	Frequent
Chronic productive cough	Common	Uncommon
Breathlessness	Persistent and progressive	Variable
Nocturnal awakening with breathlessness and/or wheezing	Infrequent	Frequent
Significant diurnal or day to day variability of symptoms	Uncommon	Common

4. Asthma management

The treatment of asthma includes avoiding exposure to triggering factors in case of allergic asthma. It also entails administrating suitable pharmacological therapy, which includes prophylactic measures to reduce inflammation and airway resistance, as well as to maintain airflow with specific acute exacerbation interventions. Corticosteroids, leukotriene inhibitors, and mast cell stabilizers are used to minimize airway inflammation by preventing the production of chemical mediators from mast cells. Bronchodilators, including xanthines (such as theophylline), antimuscarinic agents (such as ipratropium and tiotropium), and β2-adrenergic agonists (such as salbutamol and terbutaline), can be used for their bronchodilating effect.

The British Thoracic Society (BTS) has developed guidelines that highlight the recommended steps for asthma management. These guidelines are briefly summarized in **Figure 5**.

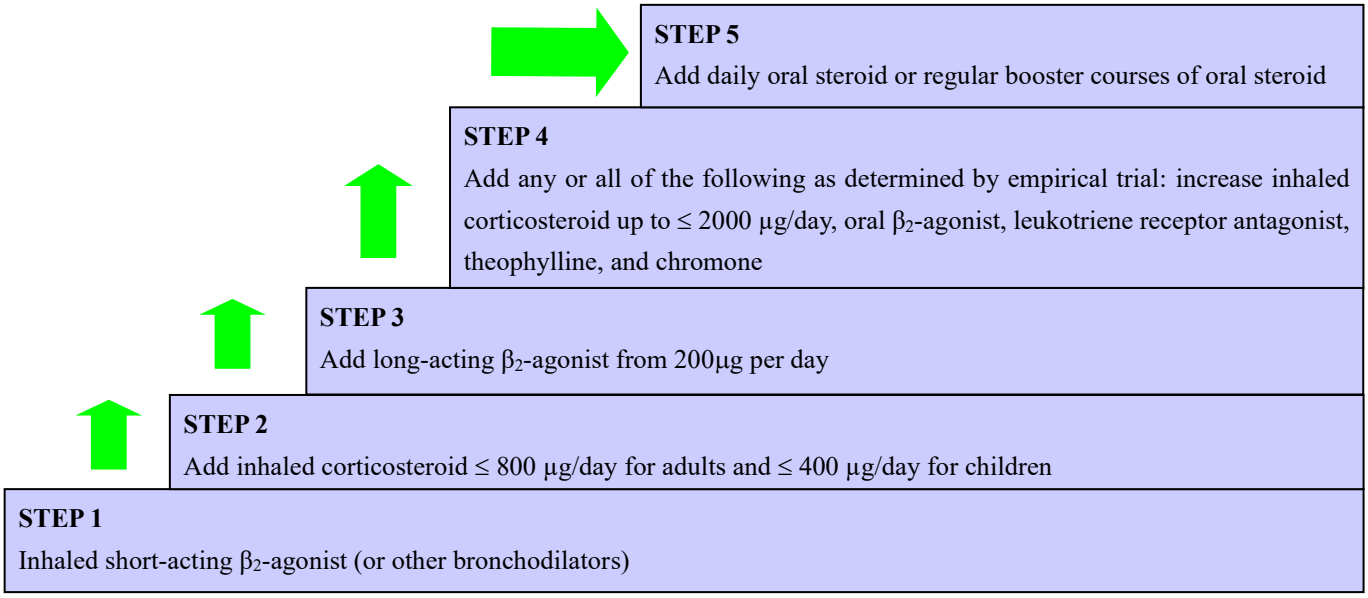

Figure 5. Step-by-step guidelines proposed by BTS/SIGN for asthma management

For **Step 1**, the guidelines recommended that SABA (such as salbutamol and terbutaline) should be administered via inhalation to relieve symptoms by rendering airways open. There is no substantial benefit to taking SABA on a regular basis (4 times per day) as compared to using it when necessary [16,17]. The pro re nata (PRN) use of SABA is strongly recommended, unless asthmatic patients show significant improvement from using SABA regularly. The consumption of two or more β_2-agonist inhaled canisters

monthly or more than 10-12 puffs daily is an indicator of poor asthma control [18]. In case of patients who use SABA, the regular use of accompanying steroidal anti-inflammatory medication is recommended.

Step 2 discusses the possibilities of reducing symptoms, improving lung functions, and preventing severe attacks, with the aid of an acceptable safety profile. Inhaled corticosteroids are the most effective drugs for assisting asthmatic patients in reaching their treatment goals [19,20]. No definite threshold for using ICS has been determined till now. The results of two recent studies confirmed the benefit from using inhaled steroids on a regular basis in mild asthmatic patients [21,22]. It is recommended that ICS should be used by patients who have any of the following indications [1]:

(1) experiencing asthma exacerbations within the last two years;
(2) using SABA three times or more per week;
(3) experiencing asthma symptoms three times or more per week or having nocturnal awakening one night per week.

In the treatment of asthma, the lowest effective ICS dose should be used. Previous studies have shown that using ICS twice daily has a higher efficacy than once daily [23]. Some recent ICS medications are pharmacologically adapted to be administered once daily, such as ciclesonide.

Step 3 is concerned with using an add-on therapy in combination with corticosteroids. The consumption of high doses of steroids may lead to many side effects. Hence, the guidelines recommended the use of add-on medications before making the decision to increase the steroid dose in an attempt to achieve better asthma control.

The first recommended alternative choice is a long acting β_2-agonist (LABA), such as formoterol or salmeterol, to enhance lung functions and reduce exacerbations [24]. The use of LABA should always be accompanied with the use of an inhaled steroid; it is not recommended to use LABA alone in the treatment of asthma.

Step 4 provides recommendations to increase the corticosteroid dose if asthma is poorly controlled based on a regimen of moderate ICS dose and add-on therapy. If the patient responds well to LABA but still has poor asthma control, the ICS dose should be increased, with the continuation of LABA. If asthma is still poorly controlled after the addition of add-on therapy, then it is recommended to use one of the following medications: leukotriene receptor antagonist, theophylline, or slow-release β_2-agonist tablets [24]. The maximum recommended dose of corticosteroid is 2,000 μg of beclomethasone daily.

Step 5 recommends using oral corticosteroids with the lowest available dose for adequate asthma control. A dose of 2000 μg of ICS daily is recommended. It is also recommended to consider other treatment options in order to limit the use of oral corticosteroids.

The guidelines emphasized the importance of evaluating the patient's inhalation technique using the prescribed inhaler and the patient's adherence to medications before stepping up the treatment plan.

5. Management of COPD

COPD is usually diagnosed by the presence of emphysema or chronic bronchitis. Many patients have both manifestations.

The goals of COPD management are as follows:

(1) to reach early and optimum diagnosis;
(2) to achieve better control of symptoms;
(3) to stop deterioration;
(4) to prevent complications;
(5) to enhance the patient's quality of life.

5.1. Diagnosis and assessment

COPD causes a reduction in peak expiratory flow (PEF) and forced expiratory volume in one second (FEV_1). According to BTS/NICE Guidelines, COPD can be classified according to severity: mild COPD, moderate COPD, and severe COPD (**Table 3**). This classification is based on the measurement of FEV_1.

Table 3. Guidelines for determining the degree of severity of chronic obstructive pulmonary disease

Disease severity	FEV_1 % predicted	Symptoms and signs
Mild	≥80	No abnormal signs Coughing exacerbated by smoking Little or no shortness of breath
Moderate	< 50	Shortness of breath alone or accompanied with wheezing during moderate exercise Coughing with or without sputum Abnormal signs, such as general reduction in breath sounds and presence of wheezing
Severe	< 30	Shortness of breath at rest or accompanied with exercise Wheezing and coughing are usually common Excessive lung inflation accompanied with cyanosis, peripheral fluid retention, and polycythaemia in advanced disease, particularly during acute attacks

Despite the fact that COPD is an irreversible disease, conducting a reversibility test is essential in confirming the diagnosis and tracking its prognosis in order to determine the most suitable and effective treatment approach. Hence, the result from this test should be clearly documented and kept in such a way that it is easily accessible when needed for future reference. COPD patients who respond significantly (show improvement) to ICS treatment are those who have an element of reversibility.

The reversibility test should be done for all COPD patients to identify those who show an increase in FEV_1 after bronchodilator inhalation. FEV_1 should be measured either before and 15 minutes after receiving nebulized salbutamol (5-5 mg) or terbutaline (5-10 mg), or before and 30 minutes after receiving nebulised ipratropium bromide (500 µg). This test is indicated for patients who are clinically stable but contraindicated for those who have comorbid infections. Six hours and twelve hours before the test, patients should avoid taking short-acting bronchodilators and LABA medications, respectively. Sustained-release theophylline should be avoided on the day before the reversibility test. The reversibility test is considered significant when the FEV_1 value increases by more than 200 ml or 15% above the value recorded before bronchodilation.

5.2. Treatment of stable COPD

The schematic diagram for managing stable COPD patients by NICE guidelines is shown in **Figure 6**.

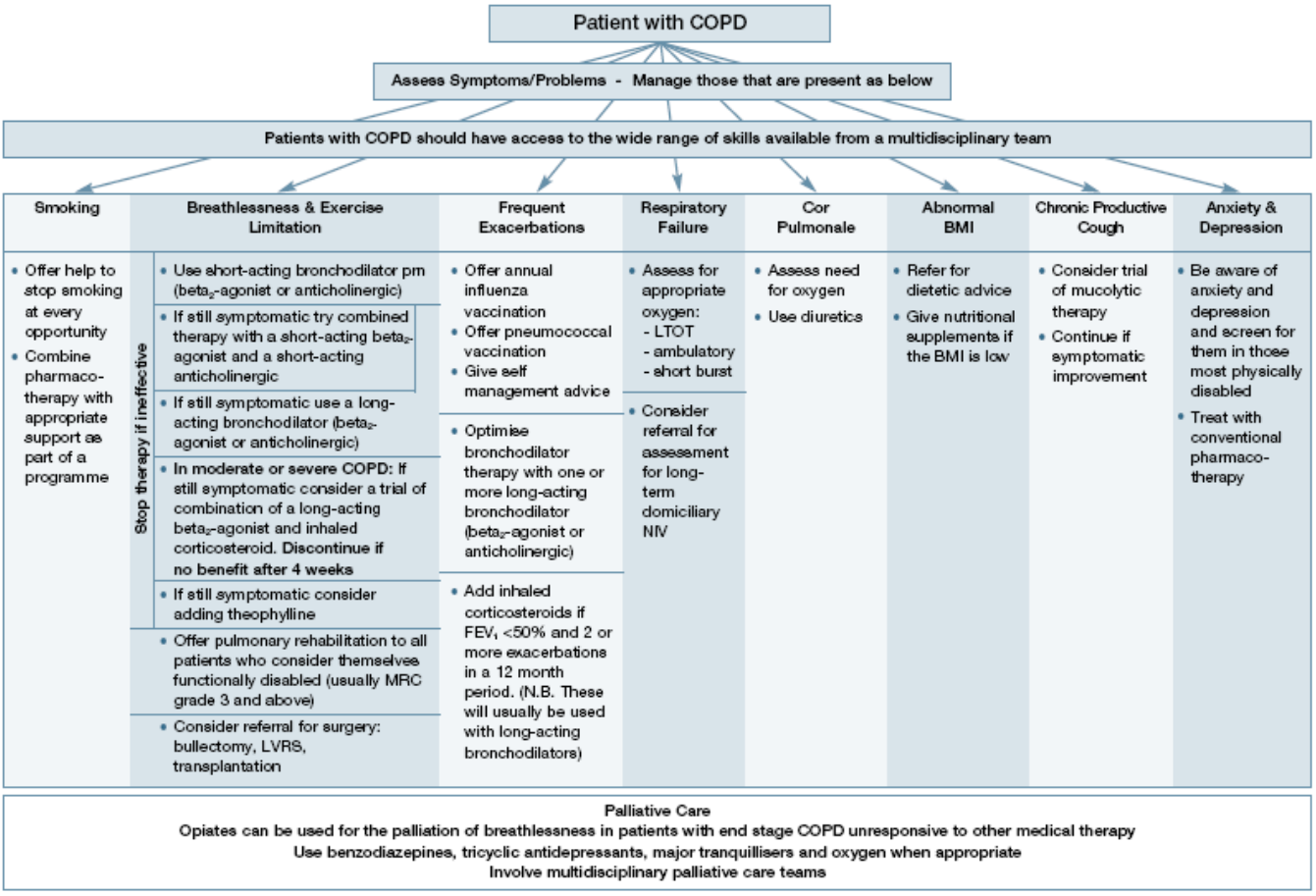

Figure 6. Recommendations for managing stable COPD patients

5.2.1. Smoking cessation

All patients with COPD should be advised on the benefits of smoking cessation. Stopping smoking is considered the most successful non-pharmacological approach that can be used to better achieve pharmacological treatment outcomes and to stop further pulmonary airway obstruction [3,8]. COPD patients who resume smoking will suffer from rapid deterioration of lung functions, which cannot be reversed by drugs. Although smoking cessation may not enhance lung functions, it will prevent the continuous rapid decline in 90% of cases and the production of excessive sputum [8,9].

5.2.2. Bronchodilators

Inhaled bronchodilators are found to be able to reduce symptoms even in cases when bronchodilator reversibility tests show negative results. Hence, inhaled bronchodilator is very important for all COPD patients in terms of symptom reduction [25].

Inhaled SABAs, such as salbutamol and terbutaline, have a rapid onset of action, and they are usually used for the purpose of relieving symptoms [3]. Inhaled antimuscarinics (e.g., ipratropium bromide) have the same efficacy as SABAs in COPD patients and may result in a greater and longer bronchodilatory effect. However, β_2-agonists are far better than antimuscarinics in relieving COPD symptoms as β_2-agonists have a faster onset of action.

When effective control of symptoms cannot be achieved or regular maintenance therapy is required, antimuscarinics may be added to the treatment regimen or may be substituted for SABAs. SABAs and antimuscarinics should not be used together unless the single medication does not provide enough symptom alleviation. LABA medications (e.g., salmeterol and formoterol) are also recommended in the treatment of COPD based on clinical trial evidence. The activity duration of LABA lasts between 12 and 14 hours. Long-acting beta-2 agonists can decrease mast cell mediator release, plasma exudation, and sensory nerve activation, in addition to their bronchodilatory effect [26].

The selectivity for M1 and M3 receptors is seen in long-acting antimuscarinic bronchodilators. Tiotropium bromide, which is the first of a new class of selective and long-acting antimuscarinics, was approved to be used once daily as a maintenance treatment for COPD patients. Compared with using a single therapy, the combination of LABA and tiotropium bromide showed additional effects in terms of daytime improvements in lung functions and the persistence of those improvements into the night, despite the once daily dosage [27-29]. According to NICE/BTS guidelines, all patients who are diagnosed with moderate to severe COPD should be prescribed with two long-acting bronchodilators but with each drug having different mechanisms of action. The cause for using anticholinergics together with β_2-agonists is that anticholinergics will reduce the vagal tone present in COPD patients, and this will result in the relaxation of airways, thus improving bronchodilation when β_2-receptors are provoked. A combination of tiotropium and formoterol was found to be more efficacious than the use of a single drug alone in terms of bronchodilation [27-29].

There is limited evidence that theophylline is beneficial in COPD. Furthermore, theophylline is known to have the potential to cause major adverse effects even at low doses. Concomitant medication therapy may enhance these effects (e.g., erythromycin and quinolone). When the peak blood concentration of theophylline exceeds 20 mg, adverse effects such as nausea, vomiting, and headache, can occur. Adverse effects such as nausea, vomiting, stomach discomfort, headache, cardiac arrhythmias, and persistent seizures become more common as its peak serum concentration levels rise. Therefore, the use of theophylline is, in fact, not recommended and should only be reserved for cases when other treatments have failed to control the symptoms. Mucolytics have garnered a lot of attention lately, and they should be considered when treating those who have long-term productive cough. The treatment goal is to reduce coughing and sputum output. According to a meta-analysis, the administration of those drugs for more than two months resulted in a 29% reduction in exacerbations when compared to placebo [30].

5.2.3. Corticosteroids

The airway obstruction in COPD is caused by many factors. Neutrophilic airway inflammation is considered one of the main factors [31]. Other factors such as protease-antiprotease imbalance [32], oxidative stress [33], and recurrent infections are also responsible for airway obstruction in COPD patients. These factors are correlated with each other, in which the inhibition of one factor may inhibit other factors in return.

The lungs of tobacco smokers usually have a higher number of neutrophils compared to non-smokers. Cigarette smoke may attract neutrophils to migrate to the lungs by stimulating alveolar macrophages to release a strong chemotactic factor [34]. Those excessive neutrophils are responsible for the fast deterioration in FEV_1 [31]. Moreover, neutrophil activation markers are increased in the sputum supernatants of COPD patients [35]. This validates that neutrophils are potent contributors in the inflammation process occurring in pulmonary airways.

There is an ongoing debate on the benefits of using inhaled or oral steroids for patients with stable COPD. While steroids have no influence on neutrophilic airway inflammation, they may have an effect on the amount of cytokines produced [36].

In COPD patients screened from the general population, inhaled budesonide was found to have no therapeutic benefit [37]. Despite the positive findings from ISOLDE trial [38], TORCH (TOwards a Revolution in COPD Health) study revealed no benefits from using inhaled fluticasone [39]. COPD patients who scored positive in the reversibility test should only be treated with ICS without the need for additional LABA. It has also been noted that the combination of ICS and LABA in a same single inhaler has enhanced lung functions and decreased the severity of dyspnea in COPD patients [40]. The aforementioned conclusions are all supported and published by the TORCH study [39]. The combination of budesonide and formoterol has been found to be beneficial according to another similar research [41]. NICE guidelines recommended that COPD patients who have FEV_1 less than 50% and are experiencing two or more attacks yearly should be given a high dose of ICS in combination with their prescribed LABA. The prescription license for Seretide (fluticasone and salmeterol) was recently updated based on the findings from the TORCH study. This enabled patients with a FEV_1 of less than 60% to be prescribed with this inhaled combined formulation.

In addition, the benefit from using LABA combined with ICS in the same MDI has been validated by a study [42]. The study showed that there is a significant co-association between salmeterol and fluticasone propionate particles, resulting in raised co-deposition when both drugs are inhaled from the same inhaler. This provides an opportunity for synergistic interaction between both drugs in the airways [43] and may be considered as an indicator for the better clinical effect observed compared to that when each drug is given individually from a separate inhaler [42].

Moreover, patients with COPD may develop cor pulmonale, which is a secondary heart disease, in addition to pulmonary hypertension, right ventricular hypertrophy, and right-sided heart failure. COPD patients usually develop acute attacks, which may require hospitalizations [37]. In this case, there will be a compromise in the choice of treatment. Antibiotics and oxygen therapy should be combined with suitable treatment of any concomitant cardiovascular disorders [9,37,44].

5.2.4. Supplemental long-term oxygen therapy (LTOT)

Supplemental long-term oxygen therapy (LTOT) enhances survival rates, activity, sleep, and mental performance in case of patients with hypoxia [4,45]. As the acid-base profile is usually compromised, arterial blood gas (ABG) analysis is regarded as the best approach for determining oxygen requirement. Arterial oxygen saturation measured by pulse oximetry (SpO_2) can also be used to determine the oxygen requirement. The physiological indications for oxygen include an arterial oxygen tension (PaO_2) of less than 7.3 kPa (55 mmHg). The goal of the treatment is to keep the oxygen saturation level (SpO_2) to more than 90% during rest, while sleeping, and while exercising. Generally, the prevention of tissue hypoxia can overcome the risk of CO_2 retention. Acidemia should be monitored if the patient develops CO_2 retention. When acidemia occurs, mechanical ventilation becomes a must for the survival of the patient.

Mechanical ventilation can be categorized as non-invasive or invasive ventilation. Non-invasive ventilation is the preferred choice whenever possible. Mechanical ventilation is not considered a treatment, but it acts as a form of life support until the underlying cause of respiratory failure is treated medically [1]. ABGs should be measured in patients who are being considered for mechanical ventilation.

When there is acidosis (pH 7.35) and hypercapnia [PaCO2 > 6-8 kPa (45-60 mmHg)] with a respiratory rate of more than 24 breaths per minute despite appropriate medical therapy and oxygen delivery, mechanical ventilation should be performed.

Non-invasive mechanical ventilation (NIV) can be classified into two types according to the methods used: non-invasive positive pressure (NPPV) (by using nasal or face masks), and negative pressure ventilation (NPV), such as iron lung (however, it is not recommended). It is worth mentioning that the most popular method is NPPV. It is mainly introduced in the form of combining continuous positive airway pressure (CPAP) and pressure support ventilation (PSV) [1, 46-49]. During the first hour of NPPV, the same

level of supervision provided in the case of conventional mechanical ventilation will be required. NPPV is contraindicated in the following cases: respiratory arrest, cardiovascular instability, mental status alterations, sleepiness, inability to cooperate, high risk of aspiration due to viscous secretions, having recent facial or gastroesophageal surgery, facial trauma, fixed nasopharyngeal abnormality, burns, and being overweight [50]. The success of NPPV can be measured by the improvement of ABGs and pH values, the alleviation of shortness of breath, the resolution of acute episodes without the need for endotracheal intubation, the termination of mechanical ventilation, and patient discharge.

6. Conclusion

Asthma and COPD are the most prevalent obstructive pulmonary diseases all over the world. Asthma and COPD share some similar symptoms, such as coughing and wheezing; however, they differ in terms of etiology, onset, frequency of symptoms, reversibility of airway obstruction, and treatment approach. In spite of that, COPD is often misdiagnosed with asthma by many chest physicians.

The primary goal of asthma management is to prevent exposure to irritating factors that trigger asthmatic symptoms. Asthma and chronic obstructive pulmonary disease significantly improve with treatment approaches such as smoking cessation and medications that open the airways (bronchodilators). However, lung functions can be fully preserved only in asthmatic patients, and not in COPD patients. According to the guidelines, the selection of treatment regimen in both asthma and COPD depends on the degree of severity. The treatment options are as follows: SABA, which cannot be used singly but only in combination with other anti-inflammatory medications; anti-inflammatory drugs, such as ICS or OCS (in severe cases); LABA; and leukotriene receptor antagonist (LTRA). Lung functions deteriorate more rapidly in COPD patients than in asthmatic patients. Supplemental long-term oxygen therapy (LTOT) is very beneficial for hypoxic patients for the early prevention of developing acidemia. Once acidemia occurs, patients should be considered for mechanical ventilation (invasive or non-invasive) in order to preserve their lives. Non-invasive positive pressure (NPPV) is considered the most commonly used non-invasive mechanical ventilation.

Disclosure statement

The authors declare no conflict of interest.

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