Abstract

Chronic pulmonary obstructive disease (COPD) is a preventable and treatable respiratory pathology, characterized by airflow limitation. The treatment has recently forwarded with the introduction of new drugs, queries about insertion of inhaled corticosteroids and future association of bronchodilations. The most distressing symptoms for patients who have COPD are dyspnea, exercise intolerance, and the progressive inability to engage in day-to-day activities. These clinical manifestations of COPD ultimately lead to poor health-related quality of life. As with many other chronic diseases, a multimodality approach to the of COPD is management advocated in several published, evidence-based guidelines. The main goals of COPD management are focused on relieving symptoms, improving health status, preventing lung function decline, improving exercise performance, preventing exacerbations, and decreasing mortality. Furthermore, these goals should be reached with minimal side effects from treatment. Traditional COPD therapies have focused on symptom control with the aim of relieving both problems of reduced airflow and declining lung function. Current medications used for COPD can reduce or abolish symptoms and the number and severity of exacerbations and can improve exercise capacity and health status. Current pharmacotherapy aims at improvement of symptoms, exercise tolerance, and health status and decrease in exacerbations. Prevention of disease progression and reduction in mortality are the ultimate goals of such therapy. All symptomatic patients who have COPD should receive pharmacologic intervention.

Keywords: Pulmonary disease, chronic obstructive; Therapeutics.

Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity worldwide. The World Health Organization (WHO) estimates that 65 million people worldwide have...
COPD of moderate to severe intensity and that by 2020, COPD will be the third leading cause of death. The main cause of this disease is active smoking, which makes COPD the most prevalent preventable disease.\(^1\)

Despite being grouped as patients of a single disease, those with COPD may exhibit distinct phenotypes of this condition, causing variable degrees of risk of exacerbation and decline in lung function.

The management of patients with COPD can be divided into 2 major methods of approach: measures for patients with stable disease and measures to be adopted during exacerbations. According to the Global Obstructive Lung Disease (GOLD) document, which was updated in 2011, patients with COPD should be categorized according to their symptoms and the risk of exacerbations, hospitalization, and disease progression.

Symptoms can be assessed by the modified Medical Research Council (mMRC) dyspnea scale (table 1) or the COPD Assessment Test (CAT) (http://catestonline.org) (figure 1). Patients with a score of >10 on the mMRC scale or >10 on the CAT are considered symptomatic.

Risk is measured by FEV1% predicted after bronchodilator use and the number of exacerbations that the patient has had in the last year. Thus, patients with a FEV1% predicted of <50% or at least 2 exacerbations are considered at risk for disease progression. COPD patients can be divided into 4 categories of therapeutic group, namely A, B, C, and D, as shown in figure 2.

Asymptomatic patients or those with few symptoms (category A) may receive medications of short duration and only when necessary. Other patients should be advised to use long-acting bronchodilators, which can be associated with another class of bronchodilator (e.g., tiotropium and a beta 2 agonist) and/or inhaled corticosteroids in more severe patients. Patients with increased risk of exacerbation can receive roflumilast associated with bronchodilators.

Below, we have described the best approach for stable patients.

### Approach for stable COPD patients

#### Smoking cessation

Stopping smoking is the most important measure that can be adopted by a patient with COPD. Enrollment in a smoking cessation support group can be decisive for the success of this therapy. The use of drugs such as varenicline or bupropion to control nicotine abstention may also have an important impact. Patients who use bupropion are 2.16 times more likely to remain abstinent after 6 to 12 months than those using placebo. However, psychological or cognitive behavioral therapy, especially when performed in conjunction with nicotine replacement therapy or drug treatment, shows superior results. In our service, outpatient support for smoking cessation has a high success rate after 6 months of follow-up.\(^{1,2}\)

#### Anti-flu vaccination

The main program for management of COPD recommends vaccination against pneumococcal disease every 5 years and against influenza annually. Prevention of influenza reduces the risk of exacerbation of disease and mortality in COPD patients. However, a consensus on the use of antiviral drugs for patients who have early symptoms of influenza infection has not been established. When used, antiviral drugs should be initiated within the first 48h. Zanamivir may trigger bronchospasm and should be prescribed with caution in combination with broncodilators.\(^1\)

#### Respiratory rehabilitation

Rehabilitation is an important pillar in the treatment of patients with COPD and should be considered for all patients with any degree of disability. If the patient cannot be enrolled into a pulmonary rehabilitation program, they should be encouraged to perform some sort of physical activity. Patients with contraindications to physical exercise, such as unstable angina or recent myocardial infarction, should
Table 1. Modified MRC dyspnea scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Symptomatology</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>I have shortness of breath when performing intense exercise</td>
</tr>
<tr>
<td>1</td>
<td>I have shortness of breath when I hasten my step, or climb stairs or a hill</td>
</tr>
<tr>
<td>2</td>
<td>I need to stop sometimes when I walk, or I walk slower than other people my age</td>
</tr>
<tr>
<td>3</td>
<td>I need to stop often due to shortness of breath when I walk around 100 meters, or for a few minutes</td>
</tr>
<tr>
<td>4</td>
<td>I am so short of breath that I do not leave the house, or need help getting dressed or bathing</td>
</tr>
</tbody>
</table>


Figure 1. Assessment involved in the CAT

Note: Table available online (http://catestonline.org).
be introduced into programs only after control of coronary disease. Owing to the importance of this topic, it will be covered in more detail in another chapter.3

Bronchodilators

Although COPD is a disease caused by obstruction that is considered irreversible, bronchodilators are a key part of the treatment of this condition. The 2 major classes of inhaled bronchodilators used are the anticholinergics and the beta 2 agonists. Inhaled drugs are preferred over oral medication because they are safe and have fewer related side effects.1,2 Patients with COPD who have respiratory symptoms should be treated with bronchodilators, preferably those with long- or very long-lasting effects, because they reduce the frequency of exacerbations and hospitalizations, improve quality of life, and reduce mortality.1,2

- Anticholinergic bronchodilators: act on the cholinergic system to block the constrictor effects of muscles in the bronchi. Ipratropium bromide is an anticholinergic with a short-duration effect and can be used in the form of a spray or nebulizer. Currently, it is used as a rescue medication, as there are also long-acting bronchodilators available. The anticholinergic tiotropium is the only long-lasting drug in this class of bronchodilators, and can be used in a single daily dose. Studies prove its superiority over placebo in the treatment of patients with stable COPD, with increased FEV1 demonstrated in patients who used this drug.1,2

- Beta 2 agonists: cause bronchodilation by acting directly on the bronchial muscle fibers. In the same way as the anticholinergics, older drugs such as salbutamol, terbutaline, and fenoterol have a short duration of action (about 4 h) and require repeat application. Therefore, they are currently reserved for rescue use or in case of worsening of dyspnea in patients with mild disease, who have infrequent dyspnea only. Patients who require frequent doses of bronchodilators may be treated with long-acting or very long-acting beta 2 agonists.1,2

Long-acting drugs such as formoterol and salmeterol exist in the form of a spray or dry powder and must be used every 12 h. Recently launched in Brazil in the form of a dry powder, indacaterol is a very long-acting beta 2 agonist that can be used in a single daily dose.

The GOLD initiative establishes the need for drug treatment of COPD based on lung function (FEV₁ % predicted) and the risk of disease exacerbation. Patients who still experience dyspnea despite the use of a bronchodilator may benefit from combination therapy with a beta 2 agonist and an anticholinergic.1,2

- Xanthines: although their mechanism of action is uncertain, the xanthines have been used in the treatment of COPD for many years. With the development of inhaled drugs, the role of xanthines was restricted due to the side effects.
that they induce, i.e., epigastric pain and nausea, as well as their interaction with other medications. Owing to its action on the diaphragm and mucociliary clearance, theophylline can be used as an auxiliary drug in the treatment of COPD. It is usually associated with inhaled medicines or used in patients of extreme age groups such as the elderly and young children.

**Inhaled corticosteroids**

Although COPD is a chronic and inflammatory disease, it is known that, unlike asthma, corticosteroids have a limited role in its control. Studies have shown that continuous use of inhaled corticosteroids in patients with stable COPD does not reduce mortality compared to placebo. Furthermore, the use of inhaled corticosteroids is associated with increased risk of pneumonia and oral candidiasis. Previous studies have not shown an increased risk of osteoporosis or cataracts, but no long-term evaluation of these conditions has been conducted. Studies suggest that continuous use of inhaled corticosteroids in combination with bronchodilators may reduce the risk of exacerbations and lung function decline. The GOLD document recommends using inhaled corticosteroids in association with bronchodilators in patients with COPD who have a FEV1% predicted of <50% (categories C and D). Calcium supplementation can be prescribed to prevent osteoporosis.1,2

**Phosphodiesterase 4 inhibitors**

Recently released in Brazil, roflumilast is an anti-inflammatory non-steroid phosphodiesterase 4 inhibitor. This enzyme metabolizes cyclic adenosine monophosphate (cAMP) and is located on the structural and inflammatory cells that participate in the inflammation involved in COPD. Roflumilast should be administered orally and since it interacts with the cytochrome P450 system, it is not advisable to use it in association with theophylline or other drugs that act on cytochrome P450.12 This drug is indicated in patients with higher risk (categories C and D), especially those with a greater frequency of exacerbation. The main side effects are nausea, diarrhea, and weight loss.

**Oxygen therapy**

Although there has been no major study on the use of supplemental oxygen in patients with COPD, it is accepted to be indicated in the presence of a PaO2 < 55 mmHg or a PaO2 between 56 and 59 mmHg in association with suggestive signs of cor pulmonale, congestive heart failure, or erythrocytosis (hematocrit > 55%). Pulmonary arterial hypertension and desaturation levels lower than 88% for at least 30% of the time spent asleep may also be considered as indications for supplementary oxygen use.3

**Nutrition**

Decreased food intake due to breathlessness, abnormal absorption as a result of hypoxemia, and high energy expenditure due to the work associated with breathing can cause weight loss in patients with COPD. Patients with a BMI below 20 are at increased risk of complications and mortality. Thus, nutritional monitoring and caloric supplementation play an important role in the treatment of these patients.

**Comorbidities**

Patients with COPD are at increased risk of cardiovascular disease, osteoporosis, respiratory infections, anxiety and depression, diabetes mellitus, and lung cancer. The evaluation of these conditions and their treatment is crucial.

**Approach during exacerbation of COPD**

Exacerbation is defined as an event in the natural course of COPD characterized by changes in the patient's baseline dyspnea and cough with or without sputum that is more frequent than the daily average, requiring changes in the therapeutic strategy used. The drugs administered in such circumstances are systemic corticosteroids and/or antibiotics. It is well established that the number of exacerbations is related to the severity of COPD and there is a decrease in
pulmonary function after exacerbation. Thus, exacerbation is related to COPD morbidity and mortality and should be promptly recognized and treated, so that the patient experiences the minimum loss of pulmonary function.

When there is an increase in the amount or a change in the viscosity or color of the sputum produced, a broad-spectrum antibiotic such as a penicillin derivative, macrolide, or quinolone is indicated. In very symptomatic patients, antibiotics can be associated oral corticosteroids such as prednisone at a dose of 20 to 40 mg/day for 2 to 5 days. Short-acting or long-acting bronchodilators may be used more frequently to relieve dyspnea. Patients who have more severe symptoms, often associated with confusion, hypotension, and severe hypoxemia, should be hospitalized. In such cases, ventilator support should be initiated using non-invasive ventilation (NIPPV) when necessary.1-5

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