Managing Patients with Chronic Obstructive Pulmonary Disease

Kronik Obstrüktif Akciğer Hastalarında Yönetim

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a treatable condition. In mild stages, smoking cessation and intermittent use of short acting bronchodilators are needed to reduce symptoms and improve prognosis. In patients with persistent symptoms, long-acting bronchodilators may be needed to reduce symptoms. In patients who have frequent or recurrent exacerbations, inhaled corticosteroids may be added to a long-acting beta-2 agonist. In such patients, pulmonary rehabilitation should also be offered. In severe disease and in patients with previous hospitalizations, a combination of inhaled corticosteroids, tiotropium and long-acting beta-2 agonists may be required to reduce morbidity. During exacerbations, patients should be treated with a short course of oral corticosteroids and antibiotics. With these measures, the health outcomes of COPD patients can be optimized.

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Key words: COPD, COPD management, smoking cessation, inhaled corticosteroids, tiotropium, long-acting beta-2 agonists, short acting bronchodilators, pulmonary rehabilitation.

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ÖZET

Kronik obstrüktif akciğer hastalığı (KOAH) tedavi edilebilir bir hastalıktır. Hafif evrelerde, semptomların giderilmesi ve prognozun düzeltilmesi amacıyla sigaranın bırakılması ve aralıklı kısa etkili bronkodilatörlerin kullanılması gerekmektedir. Sürekli semptomu olanlarda, semptomların giderilmesi için uzun etkili bronkodilatörler verilebilir. Sık veya tekrarlayan atakları olan hastalarda, inhaler kortikosteroidler uzun etkili beta-2 agonistlere eklenebilir. Bu hastalarda, pulmoner rehabilitasyon da önerilmelidir. Ağır hastalık veya önceden hospitalizasyonu olan hastalarda morbiditeyi azaltmak için inhaler kortikosteroid, tiotropium ve uzun etkili beta-2 agonistler birlikte kullanılabilir. Alevlenmeler sırasında hastalar kısa süreli oral kortikosteroid ve antibiyotiklerle tedavi edilmelidir. Bu tür önlemlerle KOAH'lı hastaların sağlıklarıyla ilgili sonuçları optimum düzeyde sağlanabilir.

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Anahtar sözcükler: KOAH, KOAH yönetimi, sigaranın bırakılması, inhaler kortikosteroidler, tiotropium, uzun etkili beta-2 agonistler, kısa etkili bronkodilatörler, pulmoner rehabilitasyon

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INTRODUCTION

Over the past decade, there has been a rapid development in the knowledge and care of patients with chronic obstructive pulmonary disease (COPD). It is now well established that COPD is a disorder which is preventable and readily treatable [1]. However, because there are many other conditions that can clinically mimic COPD, it is essential that the practicing physicians confirm the diagnosis of COPD through the use of lung function measurements. Spirometrically, COPD is defined by the presence of irreversible or minimally reversible airflow obstruction, in the absence of other conditions that give rise to airflow obstruction, such as bronchiectasis or asthma [1]. Lung function measurements can also be used to assess the severity of the disease. The most commonly used grading system is derived from the Global initiative for Chronic Obstructive Lung Disease (GOLD) consensus guidelines (Table 1) [1]. The GOLD severity classification scheme can assist the practicing physician in selecting the most appropriate therapies for their patients (see Figure 1). Generally, for patients with mild (intermittent) symptoms and with forced expiratory volume in one second (FEV_1) of 80% of predicted or greater, short acting bronchodilators can be used either intermittently or on a regular basis for symptomatic relief of dyspnea. In moderate to moderately severe disease (FEV_1 between 50 and 80% of predicted), the regular use of a long-acting bronchodilator (e.g. tiotropium or a long acting β_2 agonist) is recommended. For patients who have more than one exacerbation per year requiring oral corticosteroids and/or antibiotics, inhaled corticosteroids should be added to a long-acting bronchodilator to reduce exacerbation rates and improve health status. In severe or very severe disease (FEV_1 less than 50% of predicted), patients may require the regular use of a long-acting bronchodilator/inhaled corticosteroid combination in conjunction with tiotropium [2]. These pharmacologic therapies should be coupled with non-

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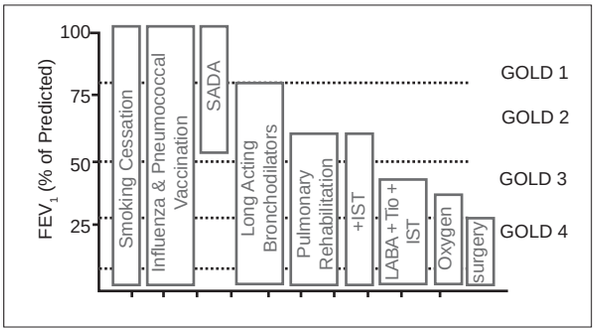

Figure 1. A Stepwise Approach To Management Of Stable Patients With COPD Definitions: FEV_1, forced expiratory volume in one second; GOLD, Global initiative of chronic Obstructive Lung Disease; IST, inhaled corticosteroids; LABA, long acting beta-2 agonists; SABA, short-acting bronchodilator

pharmacologic interventions, such as smoking cessation and pulmonary rehabilitation, to achieve the optimal results for the patients. Despite optimal therapy, patients may still experience exacerbations, which can be managed in most cases on an out-patient basis with a short course of oral corticosteroids and antibiotics. The following 4 clinical cases illustrate the contemporary approach to COPD management.

Clinical Scenarios

Patient 1 (Management of mild COPD)

A 50-year-old female office manager presents to her family physician with an early morning cough for the past year. The cough is generally dry but occasionally productive of white sputum. She is a current smoker with a 25 pack-year smoking history. She feels reasonably well and denies any significant breathlessness except during heavy exertion (e.g. jogging). She has no significant occupational history and there is no history of significant biomass exposure. She has no history of allergy, asthma, sinusitis, or respiratory infections. There is no family history of asthma or COPD. She has had no previous hospitalizations for any respiratory problems. She has no co-morbidities. The physical examination is normal. How should this patient be managed?

Based on the smoking history, the general practitioner suspects COPD and orders spirometry. When spirometry is performed, the patient's post-bronchodilator FEV_1 is 2.2 L (or 84% of predicted) and her forced vital capacity (FVC) is 3.20 L (or 98% of predicted). The FEV_1 to FVC ratio is 0.68 (or 81% of predicted). Although both FEV_1 and FVC are in the "normal" range, the reduced FEV_1 to FVC ratio (in the presence of an appropriate smoking history and symptoms) confirms objectively a diagnosis of COPD [3]. Since her post-bronchodilator FEV_1 is > 80%of predicted, the patient has mild COPD (Table 1).

Table 1. COPD staging by spirometry

COPD Stage	Spirometry (post-bronchodilator)
Mild	FEV_1 ≥80%of predicted, FEV_1/FVC <0.7
Moderate	50%≤ FEV_1 <80%of predicted, FEV_1/FVC <0.7
Severe	30%≤ FEV_1 <50%of predicted, FEV_1/FVC <0.7
Very Severe	FEV_1 <30%of predicted, FEV_1/FVC <0.7

Data Modified from reference [1]. Abbreviations: FEV_1, forced expiratory volume in one second; FVC, forced vital capacity

Management Steps

Smoking Cessation

Smoking cessation is the single most important intervention for this patient. "Will power" and physician advice can foster permanent smoking cessation in about 5%of smokers [4]. The use of lung function measurements in the discussion on smoking can enhance the rate of cessation [5]. The latter is best done by confronting the patients with their "lung age". Lung age is defined as the age of the average person who has the same FEV_1 as that of the patient and can be calculated using the formula: lung age (for men)=2.87×height (in inches)–31.25×observed FEV_1 (litres)–39.375 and lung age (for women)= age=3.56×height (in inches)–40 ×observed FEV_1 (litres)–77.28 [6]. A large randomized controlled trial has shown that smokers who received information regarding their "lung age" were twice as likely to quit as smokers who received their raw FEV_1 data [7]. At 12 months of follow-up, the cessation rate was 14% in the lung age group versus 6%in the control group.

Physician advice should, in ideal circumstances, be coupled with cognitive and behavioral modification strategies [8], which can empower patients with various coping techniques to induce and maintain smoking cessation. These techniques include distraction, positivism, relaxation, and mental imagery to modify the patient's attitude towards smoking [8] and avoidance of smoking triggers, such as drinking coffee or alcohol or associating with friends who smoke. Together, these methods are effective in fostering giving up smoking in about 10-15%of motivated smokers [9].

Nicotine replacement therapy (NRT) is also very effective in breaking the smoking habit [10]. The major goals of NRT are to reduce withdrawal symptoms, eliminate craving, and make smoking less rewarding. NRT can double the cessation rate [10]. High doses of NRT are more effective than lower doses but at the expense of more (severe) side effects [8]. However, for those patients who cannot achieve smoking cessation at lower doses, higher doses should be considered. Common side effects include insomnia, skin irritation (for patches), and early morning cravings for nicotine. There are 6 ways in which NRT can be administered: as a patch, gum, sublingual tablet, lozenge, nasal spray, or inhaler. The patches are the most common mode of delivery and are found in 16-hour (5,10,15 mg) or 24-hour (7,14,21 mg) formulations. The gums are also frequently used and they are packaged in 2 or 4 mg pieces.

Non-nicotine based drug therapies include psychotropic medications (e.g. bupropion) and $\alpha 4\beta 2$ nicotinic acetylcholine receptor agonists (e.g. varenicline) [11]. Bupropion should be prescribed at least one week before the cessation date, so that adequate blood levels can be achieved and continued for 2 to 3 months following cessation. Success rates usually range between 10 to

40%. Bupropion can be used in conjunction with nicotine replacement therapy. The common side effects of buproprion are insomnia and dry mouth. Bupropion should not be used in patients with a seizure disorder [8]. Although there are ongoing concerns regarding the possible increased risk of suicides among those who take bupropion, there is an insufficient body of evidence to support this notion. Varenicline shows great promise as an alternative to bupropion. With this drug, short-term cessation may be achieved in up to 40% of smokers. Long-term data are scarce, however, one-year cessation rates have been reported in about 20% of users [11-14]. Varenicline should be started at 0.5 mg daily while the patient is still smoking and then escalated to 1 mg per day by the second week. The patient should stop smoking completely by week 2 and the drug should be continued for another 12 weeks. Varenicline is associated with vivid (nightmares) dreams and hallucinations. Accordingly, it probably should not be used in individuals with major depression or psychosis [15].

Short Acting Bronchodilators

Since this patient experiences breathlessness only during exertion, it would be reasonable to treat her with a short-acting bronchodilator on an as needed basis (e.g. beta-2 agonists or anticholinergics). There are two major classes of short-acting bronchodilators: β_2-agonists (SABAs) and anti-cholinergic agents. SABAs have the advantage of rapid onset of action (within 1-3 minutes) [1]. Thus, they provide quick relief of dyspnea and are best used as rescue medications for patients with intermittent symptoms. If the patient developed more persistent symptoms in the future, short-acting bronchodilators may be used regularly (e.g. four times a day) or, alternatively, long-acting bronchodilators may be used. All bronchodilators work by increasing expiratory flow, reducing dynamic hyperinflation and improving exercise capacity and quality of life of patients [16]. However, the improvement in symptoms and exercise capacity is not readily predictable from the spirometric response to bronchodilators.

Vaccination

In addition to smoking cessation counseling and aids and short-acting bronchodilators, the patient should also receive pneumococcal vaccine every 5 to 10 years and yearly influenza vaccination unless contraindications exist.

Patient 2 (treatment of moderate COPD)

A 65 year old man was previously diagnosed with COPD. He is an ex-smoker (of 40 pack-years), having smoking for nearly 10 years . Today, he presents to the family physician's office complaining of being breathlessness with mild exertion (e.g. walking up a flight of stairs). A spirometry had been carried out done in the past month and it showed that the patient's FEV_1 was 1.5 L or 44% of predicted (175 cm in height). Although he is taking a combination of salbutamol and ipratropium, two puffs four times per day, he is still short of breath when walking more than 100 meters or walking up a short flight of stairs. He occasionally needs some antibiotics when he gets an upper respiratory tract infection in the Winter when his breathlessness and cough worsen. What additional treatments are needed?

In this patient, short-acting bronchodilators are no longer fully able to treat his symptoms. The patient requires long-acting bronchodilators [17]. There is, however, insufficient evidence to recommend one class of long-acting bronchodilators over another class. One approach is to treat this patient with a long-acting beta-2 agonist such as salmeterol or formoterol around the clock. Alternatively, the patient may be treated with a long-acting anticholinergic agent such as tiotropium. The recently completed TORCH and UPLIFT data indicate that both classes of drugs are effective in reducing breathlessness, improving lung function and reducing the risk of exacerbations [18,19]. It is unequivocal that tiotropium does not change the rate of decline in lung function [19]. The TORCH study suggests that salmeterol has a very modest but significant effect in slowing down the rate of progression in FEV_1 over a 3-year period [18]. The clinical relevance of this observation, however, is uncertain.

Since the patient has also had several exacerbation episodes, one can build an argument for using a combination of inhaled corticosteroid and long-acting beta-2 agonist. The TORCH study [18] indicates that this combination is more effective in enhancing lung function, reducing patient symptoms and exacerbations and decelerating the rate of decline in lung function than the individual components alone or placebo. Although controversial, the totality of data indicates that the combination therapy improves survival in moderate to severe COPD [18].

Thus, in this patient, the practicing clinician can decide to treat the patient with a long-acting bronchodilator or a combination of inhaled corticosteroids and long-acting beta-2 agonists. There is a paucity of comparative studies to determine which strategy is optimal. The only large randomized controlled trial to date showed that rates of exacerbation between the two strategies were equivalent. However, there were fewer deaths in the arm treated with salmeterol/fluticasone combination than in the tiotropium arm [20]. Thus, in this patient, in addition to influenza and pneumococcal vaccination and short-acting bronchodilators, a combination therapy with an inhaled corticosteroid and a long acting beta 2 agonist can be provided. The alternative would be to use tiotropium in lieu of the combination therapy.

Patient 3 (Management of severe COPD)

A 70 year-old man has had very severe COPD for 5 years. His FEV_1 is 0.9 L (30% of predicted). He is currently taking fluticasone/salmeterol combination and ipratropium around the clock. He stopped smoking 2 years ago but he has breathlessness at rest even on these medications. He has had 2 hospitalizations for COPD in the last 5 years and had to be on oral corticosteroids on two dif-

ferent occasions over the past year. What treatment should be recommended for this patient?

The Canadian Optimal Study showed that adding combination therapy (inhaled corticosteroids/long-acting beta-2 agonist) to tiotropium reduced the rate of hospitalization for COPD by 47% compared to tiotropium alone [2] and these patients had a better quality of life and improved lung function compared to patients taking tiotropium alone [2]. Taken together, these data indicate that, for patients with severe COPD (FEV_1 less than 50%of predicted) and with recurrent exacerbations, tiotropium in conjunction with a combination of inhaled corticosteroid and long-acting β_2 agonist should be considered. At this current time, chronic (long-term) oral corticosteroid therapy is generally not recommended because of the side effects. Oral corticosteroids should be reserved for short durations during exacerbations. Oral theophyllines should not be used because of their narrow therapeutic window and toxicity profile. Thus, this patient should be treated with a combination of inhaled corticosteroid and long acting beta-2 agonist, plus tiotropium.

In addition to these drug therapies, the patient should be vaccinated with both pneumococcal and influenza vaccines and undergo pulmonary rehabilitation. Although the contents of pulmonary rehabilitation programs vary from site to site, most rehabilitation programs teach patients about the disease, and provide structured exercise training consisting of both aerobic and strength exercises (e.g. stationary leg cycling for about 30 minutes per session, targeting 80% of patient's peak work capacity and weight training using sand bags, elastic bands and dumb-bells for 30 minutes, all 3x per week) [21]. Each session is about 3 to 4 hours in duration, scheduled usually 3 times per week for 6 to 12 weeks. During these sessions, self-management strategies should also be taught to the patients. The pulmonary rehabilitation program should generally be started in a structured (usually a hospital-based) program, but after 6-12 weeks can be switched to a well-developed home based program [22].

Patient 4 (management of acute exacerbations)

A 55 year old woman with COPD (FEV_1, 50% of predicted) comes to your office, complaining of cough (more than usual), productive of green sputum, increasing shortness of breath on exertion and mild low-grade fever for the preceding 7 days. The patient has been taking her "blue" and "green" puffers more than usual (now taking 5 or 6 times per day) and still not getting any relief from them. Her chest x-ray shows no new changes and blood counts are normal. What should be done?

The patient has an acute exacerbation of her COPD. After ruling out pneumonia and other obvious secondary causes of exacerbation (e.g. heart failure), the patient can be started on a short-course of oral corticosteroids, along with antimicrobial therapy for 7 to 10 days [23]. The choice of the antibiotic should be governed by the local resistance pattern of microbes. In most circumstances, tetracyclines, respiratory macrolides, fluroquinolones, sulpha medications, and beta-lactam antimicrobials are equally effective [23]. The optimal strength and duration of oral corticosteroids for COPD exacerbations are controversial. A reasonable choice would be 30 to 50 mg/d of oral prednisone for 7 to 10 days. . In most cases, tapering of oral corticosteroids is not required. It may take 6 to 8 weeks before the patient fully recovers. During this time, she should be monitored closely and if there is any deterioration in her health status, hospitalization should be considered.

CONCLUSION

COPD is a treatable condition. Therapy starts with smoking cessation, short acting bronchodilators (for symptom relief) and vaccinations. In patients with persistent symptoms, a combination of inhaled corticosteroids and long acting beta-2 agonists or tiotropium alone should be considered. In more advanced stages of disease, all three drugs may be required to reduce the risk of morbidity and mortality (i.e. combination of inhaled corticosteroid, long-acting beta-2 agonist, and tiotropium). In most patients with moderate to severe disease, pulmonary rehabilitation should be offered. During acute exacerbations, the patient should be treated with a short course of oral corticosteroids and antibiotics in addition to their regular inhalers.

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