abstract

Chronic Obstructive Pulmonary Disease (COPD) has been increasing in prevalence over the past several decades. The impact of COPD on the health status of Canadians will continue to be a major issue, despite declining rates of smoking, as physiologic manifestations of COPD may only be evident decades after the initiation of smoking. Given the delay between the initiation of smoking and the development of significant disease, COPD is primarily a disease of the older population. While a cure for COPD is not available, a number of medications have been noted to have a significant impact on symptoms, exercise tolerance, and quality of life.

Key words: COPD, treatment, management, older adults

Treatment of Chronic Obstructive Pulmonary Disease in Older Adults

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Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic, progressive disease that is a source of significant morbidity and mortality in the older population in Canada. COPD is a respiratory disorder largely caused by smoking and is characterized by progressive, partially reversible airway obstruction, systemic manifestations, and increasing frequency and severity of exacerbations.[1] While the primary risk factor for COPD is smoking, this disease may, on the rare occasion, be caused by occupational exposures (such as coal and grain) as well as a deficiency in alpha-1-antitrypsin.

Chronic exposure to cigarette smoke results in inflammation of the airways and initiates an inflammatory process that has not been fully characterized. However, it is known that the effect of inflammatory mediators resulting from this process persists despite the cessation of smoking. The physiological manifestation of this inflammatory process is an obstruction of expiratory airflow, both in small and large airways. The diagnosis of COPD requires spirometry (a simple test of pulmonary function) demonstrating an FEV_1 / FVC ratio of less than 0.7 and an FEV_1 of less than 80% of predicted.[2]

The deterioration of pulmonary function secondary to smoking occurs progressively over time. However, significant symptoms are often not noted until the fifth or sixth decade of life. The prevalence of diagnosed COPD increases with each decade of life (4.6% in ages 55–74 and 6.9% in individuals over 75).[3] Despite a recent decrease in the prevalence of smoking in Canada, COPD remains the only major cause of mortality whose prevalence continues to rise. This is of particular concern for females as the rate of smoking among young females has not declined as in the case of young males. As such, COPD is currently the fourth leading cause of death in Canada (Figure 1).[3] This is likely an underestimation as the listed cause of death may have been a complication of COPD, such as a respiratory infection. Thus, COPD is a significant cause of morbidity and mortality in the older population.

Therapy for COPD

Among the several therapeutic options available for COPD, only two provide a mortality benefit. These are 1) cessation of smoking, and 2) long-term home oxygen for patients who are hypoxemic.

Education and Smoking Cessation

As smoking is the primary risk factor for COPD, education and smoking cessation remain the cornerstone of management. Education not only improves the rate of smoking cessation but also allows the patient to better understand the role of specific medications during exacerbations.[4]

FEV_1 progressively decreases with age; however, smokers experience a more rapid rate of decline. The rate of decline once an individual quits smoking decreases significantly.[5] Thus, the rate of progression of COPD is slowed with smoking cessation. While quitting smoking has shown demonstrable benefit in

terms of mortality, the symptoms of COPD may persist as much of the damage caused by smoking is irreversible. Physician advice is a significant motivator for smoking cessation; as a recent trial demonstrated, a three-minute intervention encouraging cessation showed efficacy.[4]

Home Oxygen Therapy

The use of long-term home oxygen therapy in COPD has been one of the few treatments that have demonstrated a mortality benefit. The studies demonstrating efficacy were in fact carried out over 20 years ago and suggested an absolute risk reduction of 21% in mortality.[6,7] The above benefits are restricted to hypoxemic patients.

Current recommendations support the use of long-term home oxygen in patients with stable COPD and severe hypoxemia (PaO2 of 55mmHg or lower), or when the PaO2 is 60mmHg or lower in the presence of bilateral ankle edema, cor pulmonale, pulmonary hypertension, or polycythemia (hematocrit >56%).[1]

Pharmacologic Therapy of COPD

The pharmacologic therapy of COPD has traditionally been viewed with a sense of nihilism. However, recent research has demonstrated a significant improvement in lung function, dyspnea, and quality of life with a number of medications. As described in a recent consensus statement by the Canadian Thoracic Society, the treatment of COPD can be viewed in a stepwise approach (Figure 2).[1] As the severity of disease worsens, therapy can appropriately be increased to allow the patient to achieve a decreased frequency of exacerbations and improved quality of life.

The goals of pharmacotherapy of COPD are to improve dyspnea, hyperinflation, and exercise tolerance, as well as quality of life. The major classes of medications available for treatment of COPD include the bronchodilators, inhaled steroids, and combination products containing them.

1. Bronchodilators

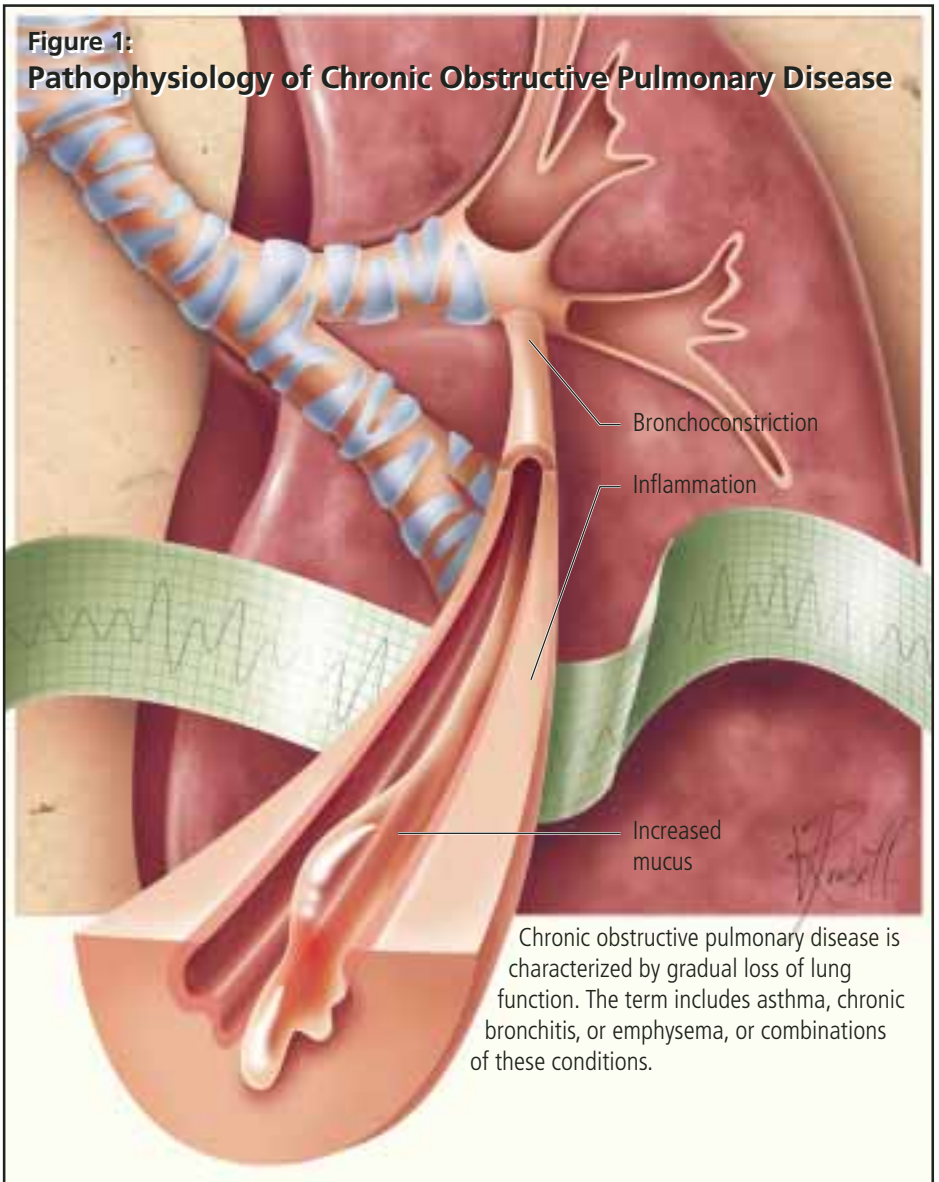
This class of medication acts directly on the smooth muscle of both small and large airways to cause smooth muscle relaxation and subsequent dilatation of the airways. The three major classes of bronchodilators include beta-2 agonists, anticholinergics, and methylxanthines.

Beta-2 Agonists

Beta-2 agonists act directly on beta-2 receptors situated on bronchiole smooth muscle. This results in bronchodilation and subsequent improvement in objective measures of airway function, exercise tolerance, and dyspnea. This class is available in short-acting (salbutamol) and long-acting (salmeterol or formoterol) preparations. Preparations of short-acting beta-2 agonists (SABAs) have long been used in the treatment of COPD. An advantage of SABAs is their rapid onset of effect. However, due to their short duration of action, they need to be taken frequently.

A number of randomized clinical trials have convincingly demonstrated the effectiveness of long-acting beta-2 agonists (LABAs) in decreasing COPD exacerbation rates and improving quality of life. These results have been confirmed by a subsequent meta-analysis.[8] Nevertheless, there is no evidence of superiority

Figure 1:
Pathophysiology of Chronic Obstructive Pulmonary Disease



Chronic obstructive pulmonary disease is characterized by gradual loss of lung function. The term includes asthma, chronic bronchitis, or emphysema, or combinations of these conditions.

of LABAs over regular use of SABAs. However, given their efficacy and ease of use, LABAs have now become one of the mainstays of treatment in patients with moderate to severe COPD.

The primary side effect of beta-2 agonists is the stimulation of the cardiovascular system, resulting in tachycardia, palpitations, and possibly hypokalemia.

Anticholinergics

Anticholinergic medications inhibit all parasympathetic activity and sympathetic cholinergic activity by blocking muscarinic receptors. The use of anticholinergic agents in the respiratory system results in both bronchodilation and a decrease in secretions. Short-acting agents such as ipratropium have been shown to be at least as effective, and sometimes more effective, bronchodilators than short-acting beta-2 agonists.[9] Furthermore, anticholinergic medications have the advantage of decreased stimulatory effects on the heart. Ipratropium is a short-acting anticholinergic drug that has a suggested dosage of two to six puffs q.i.d. Ipratropium is often administered along with salbutamol for patients with moderate or severe COPD since the bronchodilatory effects of the two medications seem to be additive.

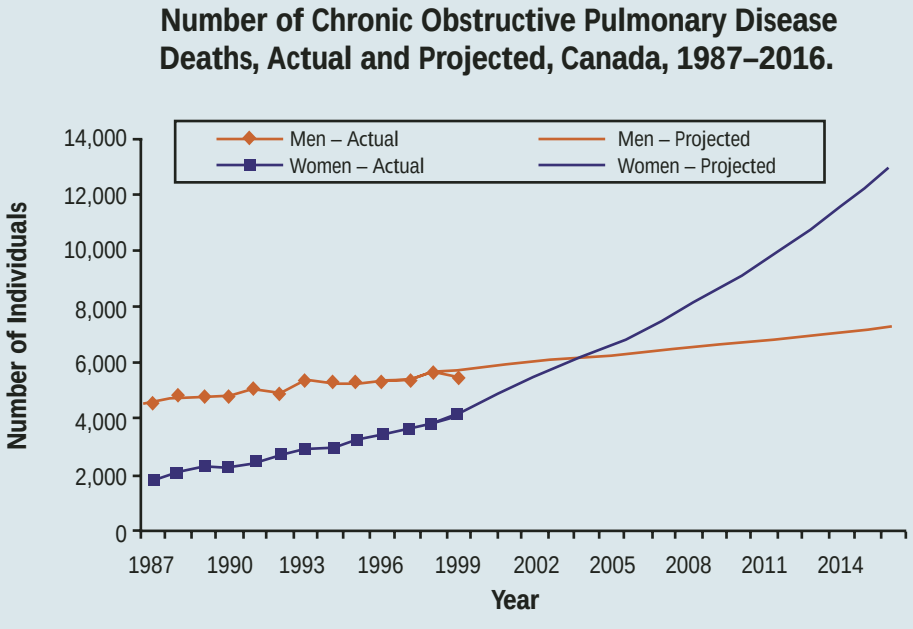
Recently, long-acting anticholinergics such as tiotropium have received widespread attention. This new medication need only be used once a day and has been demonstrated to improve both objective measurements of pulmonary function and quality of life.[10,11] A study comparing tiotropium to ipratropium demonstrated that tiotropium was associated with improved FEV_1, and fewer exacerbations.[12] A meta-analysis revealed tiotropium to be superior to ipratropium or placebo.[7] There is also some evidence that tiotropium may be superior to LABAs; however, this needs more study.[13,14]

Adverse events with these drugs are not common; however, urinary retention and glaucoma are known to be rarely associated with the use of anticholinergic medications.

Methylxanthines

The use of methylxanthines is controversial. Methylxanthines such as theophylline have been demonstrated to show a bronchodilator effect in adults; however, this effect is highly variable between patients. The primary concern with methylxanthines is a very narrow therapeutic index. In fact, theophylline levels are very unreliable in predicting toxicity.[15] At low levels, theophylline can cause diarrhea, dizziness, and tremor; however, at high doses, ventricular tachycardia and seizures can occur.[16] Furthermore, a large number of medications are known to affect the serum concentration of methylxanthines. This is of particular concern in older patients who take a large number of chronic medications and who may frequently receive temporary new medications for acute illnesses. This scenario increases the risk of methylxanthine toxicity. For the large majority of patients with COPD, beta-2 agonists and anticholinergics provide sufficient bronchodilation, thus avoiding the potential of methylxanthine toxicity. However, the addition of methylxanthines has been cited to be of benefit in certain patients with disease that is difficult to control.[1]

Figure 1: Mortality Trends for COPD in Canada



Source: Centre for Chronic Disease Prevention and Control, Health Canada using data from Mortality Database, Statistics Canada. Population projections from Statistics Canada.

2. Systemic (Oral) Corticosteroids

There have been a number of randomized clinical trials that have assessed the benefit of oral corticosteroids in COPD. As previously described, exposure to cigarette smoke can result in chronic inflammation of the airway, a process which theoretically may be attenuated with the use of systemic corticosteroids. While the evidence is clearly in favour of a role for systemic corticosteroids in an acute exacerbation, no benefit has been demonstrated in the treatment of chronic stable COPD. A study published in 1982 demonstrated that a subset of patients with a diagnosis of COPD tends to respond to steroids; however, the authors note that this same group of patients also tends to respond well to beta-2 agonists, suggesting that a diagnosis of asthma may not have been excluded.[17] Systemic corticosteroids have a number of known serious potential adverse effects and the accumulated evidence does not support their chronic use for COPD, a position supported by the recent Canadian Thoracic Society Guidelines.[1]

3. Inhaled Corticosteroids

Inhaled corticosteroids have long been the standard of care for the treatment of asthma. The anti-inflammatory effect of inhaled corticosteroids (ICSs) has also been thought to have potential benefit in the treatment of COPD. However, this has not been substantiated despite a number of studies addressing this question. In fact, ICSs have been found to be no better than placebo in improving pulmonary function and in slowing the disease process in COPD patients.[18,19] However, some of these studies have suggested a potential benefit in that there is a reduction in the frequency and severity of exacerbations in some patients with severe COPD who take ICSs.

Side effects include oral candidiasis (5%) and dysphonia. At higher dosages, systemic effects of adrenal suppression have also been noted to occur.[20] Given current evidence, ICSs are not suggested as first-line therapy. However, ICSs are a therapeutic option available for patients with severe COPD who have frequent exacerbations.

4. Combination Long-Acting Beta-2 Agonists and Inhaled Corticosteroids

A combination of LABAs and ICSs has been investigated in five separate clinical trials. The combination products are clearly better than placebo in improving pulmonary function, decreasing dyspnea, and improving quality of life. The trials also suggest that the combination ICS/LABA products improve pulmonary function to a slightly greater extent when compared to the LABA used alone. However, studies thus far have not shown that the combination products improve dyspnea or quality of life, or decrease exacerbation rates compared to LABAs used alone. Further studies are required to evaluate the exact role for ICS/LABA combinations for chronic therapy of COPD.[21–25] (See Figure 3 for a suggested stepwise approach to pharmacologic therapy for COPD.)

5. Respiratory Rehabilitation

Progression of disease in COPD involves physiologic changes that result in

Figure 2: Stepwise Approach to the Management of COPD

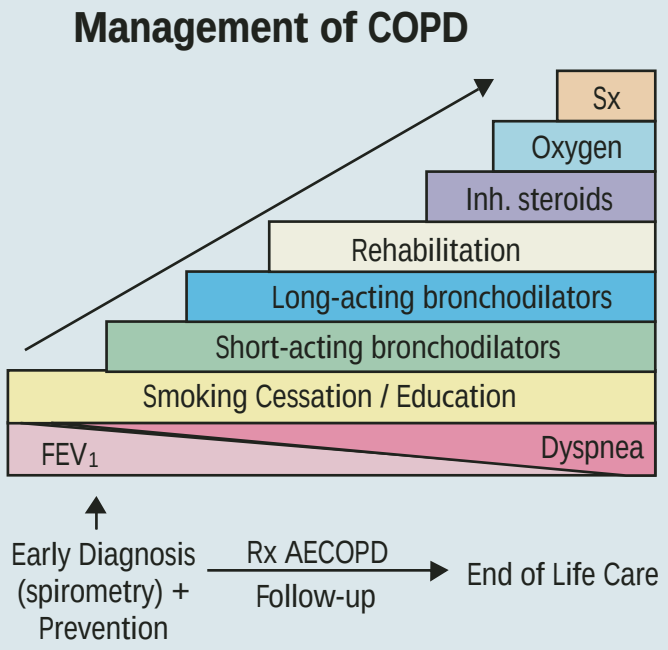


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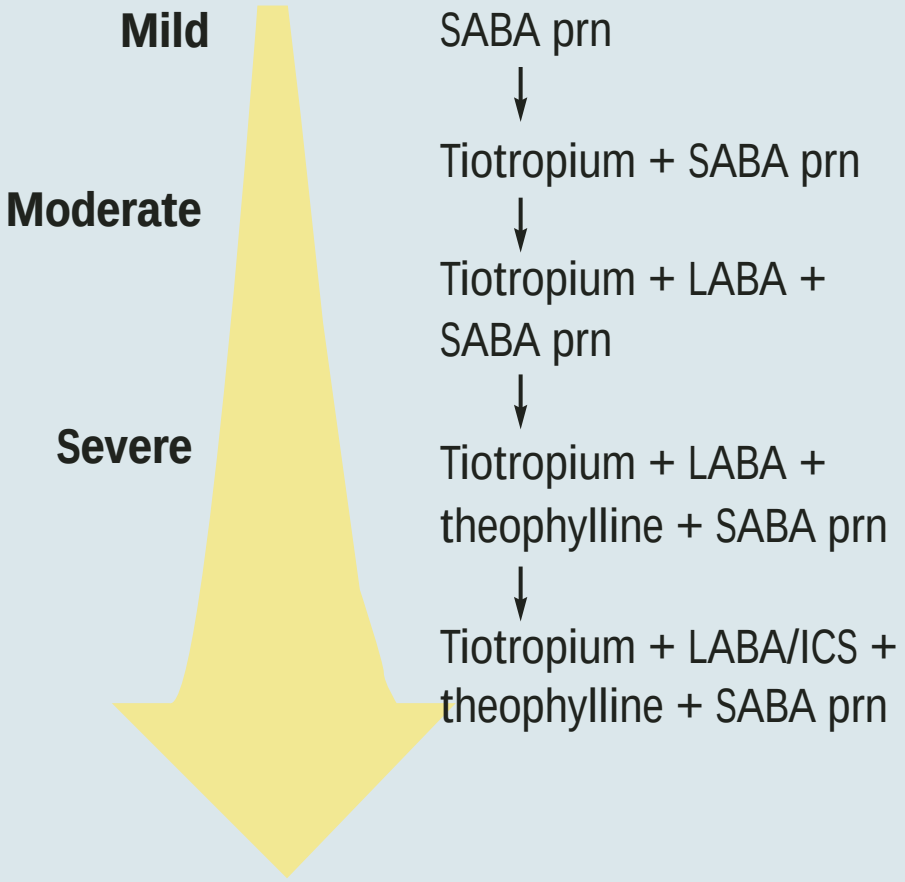
Figure 3: Suggested Stepwise Pharmacologic Therapy for COPD



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increased dyspnea. This is first noted on exertion and can often influence avoidance of any physical activity. The above series of events results in future deconditioning and, ultimately, in dyspnea at rest.

Respiratory rehabilitation consists of education, exercise training, and behaviour modification. A trial comparing rehabilitation with conventional care demonstrated significant improvements in dyspnea, walking distance, and quality of life.[26] These results were subsequently confirmed by two meta-analyses.[27,28] The Canadian Thoracic Society guidelines suggest referral to pulmonary rehabilitation for patients with stable disease, reduced activity levels, and increased dyspnea, despite pharmacologic therapy.[1]

6. Vaccinations

There is clear evidence of morbidity and mortality benefit of annual influenza vaccinations for patients with COPD.[29] The Canadian Thoracic Society recommends annual vaccinations for all patients with COPD who do not have a contraindication.[1]

Conclusion

Given the pathophysiology of the disease process in COPD, there are few interventions that will improve mortality. However, if this disease is aggressively managed with a combination of education, smoking cessation, pharmacological therapy, and respiratory rehabilitation, patients can enjoy a more symptom-free life and avoid frequent admissions to hospital for exacerbations. This has provided hope in an area of medicine traditionally viewed with therapeutic nihilism.

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