Anticholinergic Agents

The key mechanism of anticholinergic medications appears to be the blocking of muscarinic receptors (M1, M2, and M3). By blocking acetylcholine-mediated bronchoconstriction, the end result is bronchodilation.[2]

Side effects associated with anticholinergic therapy include dry mouth, glaucoma, and urinary retention.[2]

ß$_2$-Agonists

ß$_2$-agonists primarily relax airway smooth muscle by stimulating ß$_2$-adrenergic receptors. This, in turn, increases cyclic adenosine monophosphate (AMP) and produces functional antagonism to bronchoconstriction.[1]

Side effects are more frequent in oral therapy than inhaled therapy. They include palpitations and premature ventricular contractions, tremor, and sleep disturbance.[3]

Theophylline

Theophylline agents may act as nonselective phosphodiesterase inhibitors but have also been reported to have a range of nonbronchodilator actions.[1]

Theophylline requires careful dose management due to its potential toxicity and serious side effects, including ventricular and atrial rhythm disturbances and convulsions.[1]

COMBINATION BRONCHODILATOR THERAPY

- Combining bronchodilators with different mechanisms and durations of action may increase the degree of bronchodilation[1]
- The combination of a ß$_2$-agonist and an anticholinergic may produce additional improvements in lung function and health status[1]
- The safety of each component of the combination therapy should be assessed in evaluating its appropriateness for individual patients[1]

REMIND YOUR PATIENTS TO TAKE THEIR MEDICATION DAILY

CONCLUSION

For a discussion of specific bronchodilator treatment options for management of stable COPD, please refer to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Executive Summary (updated 2006) in the Guidelines and Resources section of the GOLD Web site. This is available at www.goldcopd.org.

References:

1. Global Initiative for Chronic Obstructive Lung Disease. *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease* (Updated 2006). www.goldcopd.org. Accessed March 7, 2007. **2.** Barnes PJ. The role of anticholinergics in chronic obstructive pulmonary disease. *Am J Med.* 2004;117:24S-32S. **3.** American Thoracic Society/European Respiratory Society Task Force. Standards for the diagnosis and management of patients with COPD (Internet). Version 1.2. New York: American Thoracic Society; 2004 (updated September 8, 2005). www.thoracic.org/sections/copd/resources/copddoc.pdf. Accessed March 8, 2007. **4.** Mahler DA, Wire P, Horstman D, et al. Effectiveness of fluticasone propionate and salmeterol combination delivered via the Diskus device in the treatment of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2002;166:1084-1091. **5.** Jones PW, Willits LR, Burge PS, Calverley PM. Disease severity and the effect of fluticasone propionate on chronic obstructive pulmonary disease exacerbations. *Eur Respir J.* 2003;21:68-73. **6.** Calverley P, Pauwels R, Vestbo J, et al. Combined salmeterol and fluticasone in the treatment of chronic obstructive pulmonary disease: a randomised controlled trial. *Lancet.* 2003;361:449-456.

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Managing Chronic Obstructive Pulmonary Disease (COPD)

Use of Medications in Stable COPD

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USE OF MEDICATIONS IN THE MANAGEMENT OF STABLE COPD

Although airway obstruction in COPD is only partially reversible, pharmacological treatments may[1]:

- Prevent and control symptoms
- Reduce the severity and frequency of exacerbations
- Improve health status
- Increase exercise tolerance

BRONCHODILATORS IN STABLE COPD

- Bronchodilator medications are central to symptom management in COPD[1]
- Inhaled therapy is preferred[1]
- The choice of $ß_2$-agonist, anticholinergic, theophylline, or combination therapy depends on availability and individual response in terms of symptom relief and side effects[1]
- Bronchodilators are prescribed as needed or for maintenance therapy to prevent or reduce symptoms[1]
- Long-acting inhaled bronchodilators are more effective and convenient than short-acting agents[1]
- Combining bronchodilators may improve efficacy and decrease the risk of side effects compared with increasing the dose of a single bronchodilator[1]

OTHER AGENTS

Inhaled Corticosteroids

The benefits of inhaled corticosteroids in treating COPD are much less dramatic than those seen in asthma. Their role in stable COPD management is limited to symptomatic patients with COPD with an $FEV_1 < 50\%$ predicted (Stage III: Severe COPD and Stage IV: Very Severe COPD) and in treating patients who have experienced repeated exacerbations.[1,4-6]

The dose-response relationships and long-term safety of inhaled corticosteroids in COPD are not known.[1] Inhaled steroids are not approved for use in COPD as monotherapy.

Recommended Therapy at Each Stage of COPD[a1]

COPD STAGE	Post-bronchodilator FEV_1	Short-acting Bronchodilators	Long-acting Bronchodilators	Inhaled Glucocorticosteroids
I MILD	$FEV_1 \geq 80\%$ predicted	✓		
II MODERATE	$50\% \leq FEV_1 < 80\%$ predicted	✓	✓	
III SEVERE	$30\% \leq FEV_1 < 50\%$ predicted	✓	✓	✓
IV VERY SEVERE	$FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure	✓	✓	✓

[a]COPD definition includes $FEV_1/FVC < 0.70$ and post-bronchodilator FEV_1 values as described in table.
FEV_1 = forced expiratory volume in 1 second.

Spontaneous skin bruising has been known to occur. Other topical side effects include oropharyngeal candidiasis and hoarse voice due to pharyngeal deposition.[3]

COMBINATION MEDICATIONS

Currently, only a few types of combination medications are available. The following are the most common combinations[3]:

- Short-acting $ß_2$-agonist and short-acting anticholinergic
- Long-acting $ß_2$-agonist and inhaled corticosteroid

Side effects are dependent on the medications in the combination[1] and are described on pages 3 to 5 in the specific sections for these medications.