Pharmacology

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Drugs acting on respiratory system

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Drugs acting on respiratory system

The respiratory tract is the path of air from the nose to the lungs. It is divided into two sections: **Upper Respiratory Tract** and the **Lower Respiratory Tract**. Included in the upper respiratory tract are the **Nostrils**, **Nasal Cavities**, **Pharynx**, **Epiglottis**, and the **Larynx**. The lower respiratory tract consists of the **Trachea, Bronchi**, **Bronchioles**, and the **Lungs**. The ultimate function of the respiratory system is gas exchange. This gas exchange consists of obtaining O_2 from the atmosphere and removing CO_2 from the blood. It is important to consider that O_2 is necessary for normal metabolism and CO_2 is a waste product of this metabolism. CO_2 is only inhaled in negligible quantity and thus the CO_2 we exhale is created within the body. While CO_2 plays a role in acid-base balance, it must be cleared from the body in appropriate levels through ventilation.

Asthma. Your airways narrow and make too much mucus.

Chronic obstructive pulmonary disease (COPD). This long-term condition gets worse over time. It includes bronchitis and emphysema.

Pneumonia. An infection causes inflammation in your alveoli. They might fill up with fluid or pus.

Drugs used to improve respiratory symptoms are available in inhalation and systemic formulations. These drugs include:

- beta2-adrenergic agonists
- anticholinergics
- leukotriene modifiers
- expectorants
- antitussives
- corticosteroids
- mast cell stabilizers
- methylxanthines
- mucolytics
- decongestants

1-Beta2-adrenergic agonists are used to treat symptoms associated with asthma and chronic obstructive pulmonary disease (COPD). Drugs in this class can be either short-acting or long-actin

Short-acting beta2-adrenergic agonists

Short-acting beta2-adrenergic agonists include:

- salbutamol (systemic,inhalation)
- metaproterenol (inhalation))
- terbutaline (systemic).

Long-acting beta2-adrenergic agonists

Long-acting beta2-adrenergic agonists include:

- formoterol (inhalation)
- salmeterol (inhalation).

Pharmacokinetics

Beta2-adrenergic agonists are minimally absorbed from the GI tract; inhaled forms exert their effects locally. After inhalation, beta2 adrenergic agonists appear to be absorbed over several hours from the respiratory tract. These drugs don't cross the blood-brain barrier;

they're extensively metabolized in the liver to inactive compounds and rapidly excreted in urine and stool.

Pharmacodynamics

Beta2-adrenergic agonists increase levels of cyclic adenosine monophosphate(cAMP) by stimulating the beta2-adrenergic receptors in the smooth muscle, resulting in bronchodilation. These drugs may lose their selectivity at higher doses, which can increase the risk of toxicity. Inhaled forms are preferred because they act locally in the lungs, resulting in fewer adverse reactions than systemically absorbed forms.

Adverse reactions

to long-acting beta2- adrenergic agonists include:

• tachycardia

• tremors.

A good combination

Long-acting beta2-adrenergic agonists tend to be used with anti-inflammatory agents, namely inhaled corticosteroids, to help control asthma. They're especially useful for the patient with nocturnal asthmatic symptoms.

2- Anticholinergics

Inhaled ipratropium, an *anticholinergic,* is a bronchodilator used primarily in the patient suffering from COPD, but it may also be used as an adjunct to beta2-adrenergic agonists. **Ipratropium** is the most common anticholinergic used for respiratory disorders.

Pharmacokinetics

Anticholinergics are minimally absorbed from the GI tract; they come in inhaled forms that exert their effects locally.

Pharmacodynamics

Ipratropium inhibits muscarinic receptors, which results in bronchodilation.This drug works by blocking the parasympathetic nervous system, rather than stimulating the sympathetic nervous system.

Adverse reactions to anticholinergics

The most common adverse reactions to anticholinergics include: nervousness, tachycardia , nausea and vomiting and dry mouth.

3-Corticosteroids

Corticosteroids are anti-inflammatory drugs available in inhaled and systemic forms for the short- and long-term control of asthma symptoms. Many products with differing potencies are available.

Inhaled corticosteroids include:

- beclomethasone dipropionate
- budesonide
- fluticasone
- triamcinolone acetonide.

Oral corticosteroids include:

- prednisolone
- prednisone.

I.V. corticosteroids include:

- hydrocortisone sodium succinate
- methylprednisolone sodium succinate and dexamethasone sodium phosphate.

These special populations may require special care when taking corticosteroids:

• *Children:* Growth should be monitored, especially when they're taking systemic drugs or higher doses of inhaled drugs.
• *Elderly patients:* May benefit from receiving drugs that prevent osteoporosis, such as alendronate during therapy with corticosteroids, especially if they're taking higher doses of inhaled or systemic steroids.
• *Patients with diabetes:* May require closer monitoring of their blood glucose levels while on steroids.

Pharmacokinetics

Oral prednisone is readily absorbed and extensively metabolized in the liver to the active metabolite prednisolone. The I.V. form has a rapid onset. Inhaled drugs are minimally absorbed, although absorption increases as the dosage is increased.

Pharmacodynamics

Corticosteroids work by inhibiting the production of cytokines, leukotrienes, and prostaglandins;

Inhalation for prevention

Inhaled corticosteroids are the preferred drugs for preventing future attacks in the patient with mild to severe asthma. Use of inhaled corticosteroids reduces the need for systemic steroids in many cases, thus reducing the patient's risk of developing serious long-term adverse reactions.

Systemic for the serious

Systemic forms are usually reserved for moderate to severe attacks, but they're also used in the patient with milder asthma that fails to respond to other measures. Systemic corticosteroids should be used at

the lowest effective dosage and for the shortest period possible to avoid adverse reactions.

Adverse reactions to corticosteroids

Adverse reactions to inhaled corticosteroids

may include: • mouth irritation • oral candidiasis • upper respiratory tract infection.To reduce the risk of adverse reactions from inhaled steroids, the patient should rinse out his mouth after administration.

Adverse reactions to systemic corticosteroids include

Acne, difficulty sleeping, high blood pressure, increase appetite, weight gain , increase growth of body hair, osteoporosis, GI irritation and elevation in blood glucose.

4-Leukotriene modifiers

Leukotriene modifiers are used for the prevention and long-term control of mild asthma.

Leukotriene receptor antagonists include:

• montelukast • zafirlukast.

Pharmacokinetics

Montelukast is rapidly absorbed. Zafirlukast's absorption is decreased by food, so it should be given 1 hour before or 2 hours after meals. All of the leukotriene modifiers are highly protein-bound (more than 90%).

Pharmacodynamics

Leukotrienes are substances released from mast cells, eosinophils, and basophils that can cause smooth-muscle contraction of the airways, increased permeability of the vasculature, increased secretions, and activation of other inflammatory mediators.

Leukotrienes may be inhibited by two different mechanisms.
The leukotriene receptor antagonists zafirlukast and montelukast prevent the D4 and E4 leukotrienes from interacting with their receptors, thereby blocking their action. The leukotriene formation inhibitor zileuton inhibits the production of 5-lipoxygenase, thereby preventing the formation of leukotrienes.

Adverse reactions to leukotriene modifiers

• headache • dizziness • nausea and vomiting • myalgia.

5-Methylxanthines

Methylxanthines, also called *xanthines,* are used to treat respiratory disorders.

Types of methylxanthines

Methylxanthines include *anhydrous theophylline* and its derivative salt aminophylline.
Theophylline is the most commonly prescribed oral methylxanthine. Aminophylline is preferred when an I.V. methylxanthine is required. Caffeine is also a xanthine derivative.

Pharmacokinetics

Absorption

When theophylline is given as an oral solution or a rapid-release tablet, it's absorbed rapidly and completely. High-fat meals can increase theophylline concentrations and the risk of toxicity. Absorption of some of theophylline's slow-release forms depends on the gastric pH. Food can alter absorption. When converting the patient from I.V. aminophylline to oral theophylline, the dosage is decreased by 20%.

Distribution

Theophylline is approximately 56% protein-bound in adults and 36% protein-bound in neonates. It readily crosses the placental barrier and is secreted in breast milk. Smokers and patients on dialysis may need higher doses.

Pharmacodynamics

Relax and breathe deeply

Methylxanthines decrease airway reactivity and relieve bronchospasm by relaxing bronchial smooth muscle. Theophylline is believed to inhibit phosphodiesterase, resulting in smooth-muscle relaxation, bronchodilation, and decreased inflammatory mediators.

Adverse reactions to methylxanthine

- anorexia • diarrhea • headache • tachycardia • irritability • restlessness
- dizziness.