Respiratory drugs-nursing-review

INTRODUCTION

The respiratory system includes the upper airway passages, the nasal cavities, pharynx and trachea as well as the bronchi and bronchioles. Respiration is the exchange of gases between the tissue of the body and to outside environment. It involves breathing in of an air through the respiratory tract, uptake of oxygen from the lungs, transport of oxygen through the body in the blood stream, utilization of oxygen in the metabolic activities (cells and removal of carbon dioxide from the body.

Drug therapy of pulmonary disorders is generally directed towards altering a specific physiologic function. The chapter will focus on drugs used to treat some of the more common disorders affecting the respiratory system particularly bronchial asthma, allergies and congestions associated with certain respiratory disorders.

1.1 Bronchial asthma

Asthma is physiologically characterized by increased responsiveness of the trachea and bronchi to various stimuli and by wide spread narrowing of the airways that changes in severity either spontaneously or as a result of therapy.

Impairment of airflow in bronchial asthma is caused by three bronchial abnormalities.

i. Contraction of airway smooth muscles
ii. Thickening of bronchial mucosa from edema and cellular infiltration
iii. Inspissations in the airway lumen of abnormally thick, viscid plugs of excessive mucus.

Pathogenesis

There are two types of bronchial asthma i.e extrinsic and intrinsic.

Extrinsic asthma is associated with history of allergies in childhood, family history of allergies, hay fever, or elevated IgE.

Intrinsic asthma occurs in middle-aged subjects with no family history of allergies, negative skin tests and normal serum IgE.

Immunologic model

Asthma is a disease mediated by reaginic (IgE) antibodies bound to mast cells in the airway mucosa. But not all features of asthma can be accounted for by antigen-challenge model. Nonantigenic stimuli like viral infections, exercise, and cold air stimulate bronchial spasm.

In allergic asthma, the immediate phase, i.e the initial response to allergen provocation, occurs abruptly and is due mainly to spasm of the bronchial muscle. Allergen interaction with mast cell fixed IgE release histamine, LTC4 and LTD4 which cause bronchial spasm.

PHARMACOTHERAPY OF BRONCHIAL ASTHMA

Drug used in the treatment of bronchia asthma can be grouped into three main categories:

1. Bronchodilators
   a. β- Adrenergic agonists which include:
      □ Non selective β-agonists e.g. adrenaline
      □ Selective β-agonists e.g. salbutamol
   b. Methylxanthes: theophylline derivatives
   c. Muscarinic receptor antagonists e.g. Ipratropium bromide

2. Mast cell stabilizers, e.g. cromolyn sodium, nedocromil, ketotifen

3. Antiinflammatory agents: corticosteroids

1. β- ADRENERGIC AGONISTS (SYMPATHOMIMETIC AGENTS)
   a) Non- selective- β-agonists
- Epinephrine, ephedrine, isoproterenol
b). Selective β-agonists
- Salbutamol, terbutaline, metaproterenol, salmeterol, formoterol and etc

**Mechanism of Action**
β-Agonists stimulate adenyl cyclase and increase formation of cAMP in the airway tissues. They have got several pharmacological actions important in the treatment of asthma
- Relax smooth muscles
- Inhibit release of inflammatory mediator or broncho constricting substances from mast cells.
- Inhibit microvasculature leakage
- Increase mucociliary transport

a. **Non-selective β-agonists**
- Cause more cardiac stimulation (mediated by a β1 receptor), they should be reserved for special situation.
- Epinephrine: very effective, rapidly acting bronchodilator especially preferable for the relief of acute attack of bronchial asthma.
- Administered by inhalation or subcutaneously.
Side effects include arrhythmia and worsening of angina pectoris, increase blood pressure, tremors etc

**Contraindication:** - hypertension, arrhythmia,

**Ephedrine:** compared to epinephrine, it has longer duration of action but more pronounced central effect and lower potency. It can be given orally. The drug is currently infrequently used because of development of more efficacious and beta2-selective agents.

b. **Selective β2-selective agonists**
Largely replaced non – selective β2- agonists, are effective after inhaled or oral administration and have got longer duration of action. They are the most widely used sympathomimetics.
Commonly used drugs both by oral and inhalation are Salbutamol, terbutaline, metaproterenol, pirbuterol and bitolterol.
Salmeterol and formeterol are new generation, long acting β2- selective agonists (with duration of action 12 hrs or more). These drugs appear to interact with inhaled corticosteroids to improve asthma control.
Delivery of adrenoreceptor agonists through inhalation results in the greatest local effect on airway smooth muscle with least systemic toxicity.

**Side effects**
Tremors, anxiety, insomnia, tachycardia, headache, hypertension and etc.

**Contraindications:** Sympathomimetics are contraindicated in patients with known hypersensitivity to the drugs
Precautions: They should be used cautiously in patients with hypertension, cardiac dysfunction, hyperthyroidism, glaucoma, diabetes, pregnancy.

2. **METHYLXANTHINES**
- The three important methylxanthines are theophylline, theobromine, and caffeine. The theophylline preparations most commonly used for therapeutic purposes is aminophylline (theophylline plus diethylamine).

**Mechanism of Action**
i. Competitively inhibit phosphodiesterase (PDE) enzyme leading to increased cAMP level.
ii. They competitively inhibit the action of adenosine on adenosine (A1 and A2) receptors (adenosine has been shown to cause contraction of isolated airway smooth muscle and to provoke histamine release from airway mast cells.
iii. Inhibit the release of histamines and leukotriens from the mast cells
Of the three natural xanthines, agents theophylline is most selective in its smooth muscle effect, while caffeine has the most marked central effect.

**Pharmacokinetics**
Only slightly soluble in water so has been administered as several salts containing varying amounts of theophylline base. Most preparations are well absorbed from gastro intestinal tract and metabolized by liver. Doses should be decreased in cases of liver disease and heart failure.

**Adverse Effects:**
Anorexia, nausea vomiting, abdominal discomfort, headache, anxiety, insomnia, seizures, arrhythmias
Theophylline is now largely reserved for patients in whom symptoms remain poorly controlled despite the combination of regular treatment with an inhaled anti-inflammatory agent and as needed use of a β2 agonist.

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**3. MUSCARINIC RECEPTOR ANTAGONISTS**

**Mechanism of Action**
Muscarinic antagonist competitively inhibit effect of acetylcholine at muscarinic receptors – hence block the contraction of air way smooth muscle and the increase in secretion of mucus that occurs in response to vagal activity e.g atropine sulfate
Systemic adverse effects as a result of rapid absorption include urinary retention, tachycardia, loss of accommodation and agitation and local effects like excessive dryness of mouth limits the quantity of atropine used. Ipratropium bromide is poorly absorbed and does not readily enter the central nervous system thus permits the delivery of high doses to muscarinic receptor in the airways; hence, it can safely be used for bronchial asthma.
Antimuscarinic antagonist drugs appear to be slightly less effective than β- agonists agents in reversing asthmatic bronchospasm. The addition of ipratropium enhances the bronchodilation produced by nebulized albuterol in acute sever asthma. The antimuscarinic agents appear to be of significant value in chronic obstructive pulmonary diseases - perhaps more than asthma. They are useful as alternative therapies for patients intolerant of β - agonists

**4. ANTI-INFLAMMATORY AGENTS: CORTICOSTEROIDS**
Used both for treatment and prophylactic purposes

**Mechanism of action**
They are presumed to act by their broad anti inflammatory efficacy mediated in part by inhibition of production of inflammatory mediators. They also potentiate the effects of β- receptor agonists and inhibit the lymphocytic-eosinophilic airway mucosal inflammation

**Effects on airway**
- decreases bronchial reactivity
- increases airway caliber
- decreases frequency of asthma exacerbation and severity of symptoms
The corticosteroids commonly used are hydrocortisone, prednisolone, beclomethasone, triamcinolone and etc.
The drugs can be taken by inhalation as aerosol, oral, or an IV administration
Because of severe adverse effects when given chronically, oral and parenteral corticosteroids are reserved for patients who need urgent treatment and those who have not improved with a bronchodilator. Aerosol treatment is the most effective way to decrease the systemic adverse effect of corticosteroid therapy. Abrupt discontinuation should be discouraged because of the fear of adrenal insufficiency. Doses should be decreased after improvement. Regular or controlled therapy is better maintained with aerosol corticosteroids.

Clinical uses in bronchial asthma
- Urgent treatment of severe asthma not improved with bronchodilator
  o IV, inhalation or oral.
- Nocturnal asthma prevention
  o oral or inhalation
- Chronic asthma
  o Regular aerosol corticosteroids

Side effects:
- Suppression of the hypothalamic-pituitary-adrenal axis
- Osteoporosis
- Sodium retention and hypertension
- Cataract
- Impairment of growth in children
- Susceptibility to infection like oral candidiasis, tuberculosis

5. MAST CELL STABILIZERS
  e.g. cromolyn sodium

Mechanism of action
Stabilize the mast cells so that release of histamine and other mediators is inhibited through alteration in the function of delayed chloride channel in cell membrane. It has no role once mediator is released and is used for casual prophylaxis.

Clinical uses
- Exercise and antigen induced asthma
- Occupational asthma

Side effects
Poorly absorbed so minimal side effect
Throat irritation, cough, dryness of mouth, chest tightness and wheezing

TREATMENT OF STATUS ASTHMATICS

Status asthmatics
Very severe and sustained attack of asthma which fails to respond to treatment with usual measures
Management includes:
- Administration of oxygen
- Frequent or continuous administration of aerosolized B2 agonists like salbutamol
- Systemic corticosteroid like methyl prednisolone or hydrocortisone IV
- Aminophylline IV infusion
- IV fluid to avoid dehydration
- Antibiotics in the presence of evidence of infection

ANTI-TUSSIVES
Cough is a protective reflex, which serves the purpose of expelling sputum and other irritant materials from the respiratory airway.

Types:
- Useful productive cough
  o Effectively expels secretions and exudates
- Useless cough
  o Non-productive chronic cough
  o Due to smoking and local irritants

Anti-tussives are drugs used to suppress the intensity and frequency of coughing.

**Two Types of Anti-tussives:**
1. Central anti-tussives
   - Suppress the medullary cough center and may be divided into two groups:
     o Opioid antitussive e.g. codeine, hydrocodeine, etc
     o Non opioid antitussives e.g. dextromethorphan
2. Peripheral antitussives
   - Decrease the input of stimuli from the cough receptor in the respiratory passage.
     e.g: Demulcents e.g. liquorices lozenges, honey
     Local anesthetics e.g. lidocaine aerosol

**Demulcents** coat the irritated pharyngeal mucosa and exert a mild analgesic effect locally.

**CODEINE**
Codeine is a narcotic relatively less addicting drug and central antitussive agent and it’s main side effects are dryness of mouth, constipation and dependence.

**DEXTROMETROPHAN**
Dextromethorphan is an opioid synthetic antitussive, essentially free of analgesic and addictive properties and the main side effects are respiratory depression

**Expectorant** is a drug that aid in removing thick tenacious mucus from respiratory passages, e.g. Ipecac alkaloid, sodium citrate, saline expectorant, guanafenesin, potassium salts

**Mucolytics** are agents that liquefy mucus and facilitate expectoration, e.g. acetylcysteine.

**DECONGESTANTS**
Decongestants are the drugs that reduce congestion of nasal passages, which in turn open clogged nasal passages and enhances drainage of the sinuses.

**Mechanism of Action**
Mucus membrane decongestants are α1 agonists, which produce localized vasoconstriction on the small blood vessels of the nasal membrane. Reduce congestion in nasal passages.

**Clinical uses:**
Used in congestion associated with rhinitis, hay fever, allergic rhinitis and to a lesser extent common cold.

Drugs can be administered nasally or orally for longer duration of action.

**Classification:**
1. Short acting decongestants administered topically – phenylephrine, phenylpropanolamine
2. Long acting decongestants administered orally - ephedrine, pseudoephedrine, naphazoline
3. Long acting topical decongestants
   o Xylometazoline
   o oxymetazoline
Side effects:
1. Rebound nasal congestion
2. Ischemic changes in mucus membranes
3. Nasal burning, stinging, dryness
4. Tachycardia, arrhythmia, nervousness, restlessness, insomnia, blurred vision

Contraindications
1. Hypertension, severe coronary artery disease