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# DRUGS FOR ASTHMA AND OTHER RESPIRATORY DISORDERS

SUNALI MEHTA

Principal use of drugs for respiratory illness is to maintain the patency of the respiratory tract and also effective gas exchange between blood and tissues.

Obstruction to airflow can be due to:

Constriction of bronchioles

Excessive mucous secretion

Oedema

Problems can arise at any stage of the respiratory tract from the nasal cavity to the alveoli and can be of any kind – infection, immune response, inflammatory.

Drugs used in the treatment of the lower respiratory tract include:

Bronchodilators

Inhaled corticosteroids

Prophylactics

Leukotrine receptor antagonists

Oxygen therapy

Respiratory stimulants

Surfactants

Obstructive airways disease are characterized by restricted expiratory airflow. Bronchial asthma is a reversible condition caused by bronchospasm, mucus hypersecretion and oedema.

There are two forms of asthma they are extrinsic and intrinsic.

In extrinsic asthma the onset of the disease is due to an allergen, which triggers the release of the chemical mediators from the lung tissue and these in turn induce the following effect vasodilation, inc permeability of pulmonary capillaries, viscous mucus production and severe constriction of the bronchioles. The nett change is the narrow passage of the air which allows that the air be inhaled but does not permit the air to be expelled out and hence the lungs become hyperinflated. With constant exposure to the causative agent a chronic state develops.

The tissue of the lungs are rich in mast cells, a tissue bound form of the leukocytes sub population called basophils. These play a critical role in the development of the respiratory condition with an immune basis. The cytoplasm of these cells contain granules full of inflammatory mediators, when the membrane ruptures there is a release of these chemical mediators which result in bronchoconstriction, oedema and increased mucus production. This is how it is linked to immunity.

The other form is the intrinsic type and is not triggered by allergens but is more related to an alteration in the ans function. There is an imbalance between the sns and psns stimulation of the bronchioles. Sns stimulates bronchodilation in a stressed condition thru the activation of the beta2 adrenergic receptors. Whereas the psns leads to bronchoconstriction and inc mucus production while at rest thru the activation of the muscarinic receptors. In this type the psns dominates and the airways are considered hyperactive.

Respiratory Pharmacology:

There are many drugs available which can be used to alleviate the symptoms of the respiratory conditions:

1. Bronchodilators: Asthma is characterized by narrow airways and one of the major concerns is the airway diameter in bronchoconstriction. These are also known as relievers.

One group the beta agonists stimulate the beta – adrenergic receptors on the bronchial smooth muscle. The antimuscarinic agents which block the muscarinic cholinergic receptors on the bronchial smooth muscle. Methylxanthines which inc the levels of the intracellular cAMP which modulates the cellular activity. These drugs can either be used on their own or in combination to produce an enhanced effect.

Beta – agonists:

It is the beta 2 agonists that will result in bronchodilation whereas the beta 1 is associated with the cardioacceleration which is undesirable. E.g. salbutamol, eformoterol, salmeterol the latter two are long acting beta – agonist and their effect can last upto 12 hours after inhalation. They are recommended for the stabilization of moderate persistent asthma. Common side effects are muscle tremor, palpitations, peripheral vasodilation and headache.

Ephedrine may be used and is useful in the following ways:

Leads to bronchodilation by activating the beta receptors

Reduces pulmonary vasoconstriction by the stimulation of the alfa receptors.

Antimuscarinic agents:

The synthetic atropine like antimuscarinic agents ipratropium and tiotropium block the muscarinic receptors associated with the psns stimulation and leads to bronchodilation and in theory results in less mucus production. The onset of action is slower than that of the beta agonist but the duration of the effect is prolonged. Main adverse reaction is dry mouth though after inhalation in some cases urine retention, glaucoma and pupil dilation have been reported.

### Methylxanthines:

Theophylline, aminophylline induce broncho dilation thru a mechanism that bypasses the extracellular receptors. These prevent the degradation of the cAMP by phosphodiesterase which act as a second messenger and stimulate high activity of the cell. Since there is an inc level of cAMP it leads to an inc activity of the bronchial smooth muscle and hence leading to bronchodilation. These are phosphodiesterase inhibitors. Their action is not specific and hence inc the activity of the of the muscle and nerve cells also. Adverse reactions include insomnia, anxiety, nervousness, epigastric distress, nausea, vomiting and tachycardia.

### Inhaled corticosteroids:

Are potent anti – inflammatory agents, but are associated with a serious number of toxic reactions. topical administration directly to the site of inflammation in this case the bronchial passage limits the systemic adverse reactions. they inhibit the rupture if mast cells and hence the synthesis of the inflammatory mediators is diminished and as a result new antibody formation is inhibited and the activity of the immune cell is suppressed. There is also a dec in the pathophysiological changes such as bronchoconstriction, mucus production and oedema.

Common side effect is an infection of candida albicans in the pharynx leading to a hoarse voice. These ehance the effect of the bronchodilators. Three are available and they are beclomethasone, budesonide and fluticasone.

### Use of systemic corticosteroids in asthma:

They can be used systemically also to treat asthma. They can either be given orally or IV. It reduces the severity and duration of the attack and a relapse also. Prednisolone and prednisone are used in oral therapy. Dexamethasone or hydrocortisone are agents used in the case of an acute attack. Adverse reaction include suppression of the hypothalamus – pituitary axis, hyperglycaemia, hyperkalemia, fluid retention and inc susceptibility to infection.

#### Prophylactic asthma preparations:

Sodium cromoglycate and nedocromil sodium are topical agents and can belong to preventer group of agents. They are useful in the management of asthma in children, they have also shown to reduce the frequency and severity of the acute attacks. These drugs prevent the release of chemical mediators from the mast cells, but these are not used in the case of an acute attack since the mast cells have already ruptured. Not many adverse reactions associated with these drugs. The common side effect is an unpleasant taste and respiratory tract irritation by coughing.

Leukotrine receptor antagonist: they are a novel group of antiasthma drugs. They are additional drugs used in the treatment of asthma. Leukotrienes are inflammatory mediators. They cannot be stored within the cells and are produced in response to an immune challenge. Three leukotrienes are associated with asthma and are produced by inflammatory cells, the mast cells. The large and small passage bear specific receptor for these. They trigger smooth muscle contraction, mucus secretion and oedema. The antagonist block the action of the leukotrienes in the airway alleviating the symptoms. Common side effects include headache and GI upset.

#### Respiratory stimulants:

Doxapram is a short acting IV administered respiratory stimulant for the treatment of COAD. It acts by stimulating the respiratory centers in the medulla, with improved ventilation carbon dioxide is removed from the lungs. Adverse reactions there is a general increase in the nervous system activity which include hyperactivity, disorientation, increased muscle tone, dyspnoea, diarrhea, chest tightness and palpitations.

#### Surfactants:

The walls of the alveoli are coated with a thin liquid film which assists the natural recoil of the lungs during expiration. The air sacs would completely collapse between breathes if it were not for the surfactants , they act to reduce surface tension hence keep the alveoli patent. Beracant which is used to treat the respiratory distress syndrome in infants since they do not have enough surfactant production. It is a bovine form of colfosceril along with other phospholipids. It must be administered to the trachea of the infant.

Drugs to know:

Salbutamol: beta agonist

Ipratropium: bronchodilator antimuscarinic agent

Duovent (Containing both Ipratropium and fenoterol)

Beclomethasone : inhaled corticosteroid

Prednisolone: systemic steroids

Prednisone : systemic steroids

Beracant: surfactant

Pulmozyme : mucolytic agent: treatment of cystic fibrosis : this is a recombinant human Dnase which works by cleaving the DNA strands present in the viscous bronchial secretions of the cystic fibrosis bronchioles.

Doxapram : Respiratory stimulant

Emphysema : means the loss of functioning of the lungs.