

Pharmacology team

Drugs of Asthma & COPD



Treatment of Asthma

	Bronchodilator	Anti-inflammatory
Aim of Treatment	- Quick relief medications - Treat acute episodic attack of asthma.	- Control medications or prophylactic therapy. - Reduce the frequency of attacks.
E.G	1- Short acting β 2-agonist 2- Anti-muscarinic. 3- Xanthine preparation.	1- Corticosteroids. 2- Mast cell stabilizers. 3- Leukotrienes antagonists 4- Anti-IgE monoclonal antibody 5- Long acting β 2-agonists

1st: Bronchodilators:

Name of the group	MOA	Calcification and e.g
1- Short acting β 2-agonist	<p>1- direct β2 stimulation → stimulate adenylyl cyclase → Increase cAMP → bronchodilation</p> <p>2- Inhibit mediators release from mast cells.</p> <p>3- Increase mucus clearance by (increasing ciliary activity).</p>	<p>1- Non selective β agonists: A- Epinephrin (use for acute anaphylaxis) Not effective orally because it digest by HCL in the stomach</p> <p>Contraindications Diabetes People with heart problems e.g angina</p> <p>B- Isoprenaline</p> <p>2- Selective β2 – agonists: A- Short acting β2 agonist - Salbutamol - Terbutaline Used also as tocolytics (tocolytics means when the smooth muscle begin contraction for oremature labor)</p> <p>B- Long acting β2 agonist - Salmeterol - Formeterol Used in nocturnal asthma (because it has long duration so it use to relive asthma at night (bedtime)</p>

B2 Agonists combined with corticosteroid to avoid tolerance on other word to make b2 agonist more effective

Name of the group	MOA	Pharmacokinetic	Uses	e.g
2- Anti-muscarinic (muscarinic antagonist)	<p>Inhibit bronchoconstriction and mucus secretion.</p> <p>Not selective because it work on all type of muscarinic receptors</p>	<p>1- Quaternary derivatives(that means it is polar soluble) of atropine.</p> <p>2- Given by aerosol inhalation.</p> <p>3- Does not diffuse into the blood Do not enter CNS.</p> <p>4- Delayed onset of action.</p> <p>5-Duration of action 3-5 hr</p>	<p>1- COPD</p> <p>2- acute sever asthma combined with β2 agonist + steroids.</p>	<p>1- Ipratropium:</p> <p>2- Tiotropium: - By inhalation - Ling duration (24 hr) - for COPD , WHY? Coz it's bronchodilator and decrease mucus production.</p>

Name of the group	MOA	Pharmacological Effects	e.g
3- Xanthinepreparation.	<ul style="list-style-type: none"> - phosphodiesterase inhibitors. - \uparrowcAMP \rightarrow bronchodilation - Adenosine receptors antagonists (A1) - Increase diaphragmatic contraction (improve ventilation) - Stabilization of mast cell membrane. 	<p>1- relaxation of bronchial smooth muscles.</p> <p>2- CNS stimulation.</p> <p>* stimulant effect on respiratory center. * decrease fatigue & elevate mood.</p> <p>* tremors, nervousness, insomnia, convulsion.</p> <p>It found in coffee and tea that will make you remember the effects =)</p> <p>3- Skeletal muscles : \uparrowcontraction of diaphragm \rightarrow improve ventilation</p> <p>4- CVS: + ve Inotropic (\uparrow heart contractility) + ve chronotropic (\uparrow heart rate)</p> <p>5- GIT: Increase gastric acid secretions So don't use it with people have peptic ulcer Kidney: weak diuretic action (\uparrowrenal blood flow)</p>	<p>1- Theophylline (orally – sustained release preparation- parenterally).</p> <p>2- Aminophylline (theophylline + ethylene diamine) >not important (orally – parenterally).</p>
	Pharmacokinetics	Uses	Side Effects
	<ul style="list-style-type: none"> • Metabolized in the liver by Cyt P450 enzymes (t 1/2 =8 h) T 1/2 is decreased by Enzyme inducers (phenobarbitone-rifampicin) T1/2 is increased by Enzyme inhibitor (cimetidine, erythromycin) 	<p>1. second line drug in asthma (theophylline).</p> <p>2. For status asthmatics (aminophylline is given as slow infusion).</p> <p>3. COPD</p>	<ul style="list-style-type: none"> - Low therapeutic index narrow safety margin. (monitoring of theophylline blood level is necessary) CNS side effects: seizures CVS effects: hypotension, arrhythmia. GIT effects: Nausea & vomiting

2nd : Anti-inflammatory

Name of the group	MOA	Routes of administration	
<p>1- Corticosteroids. (strongest one)</p>	<ol style="list-style-type: none"> 1. Inhibition of phospholipase A2 decrease synthesis of arachidonic acid & prostaglandin and leukotrienes 2. Decrease inflammatory cells in airways e.g. macrophages, Eosinophils 3- Mast cell stabilization decrease histamine release 4- decrease capillary permeability and mucosal edema. 5- Inhibition of antigen-antibody reaction. 	<p>Inhalation (metered-dose inhaler):</p> <p>Beclomethasone Fluticasone (high first pass effect in liver & low bioavailability).= and that will be good because we do not want it to reach blood circulation .</p> <p>Orally: Prednisone Injection: Hydrocortisone Methyl prednisolone</p>	
	<p style="text-align: center;">Pharmacodynamics</p> <ul style="list-style-type: none"> - Not bronchodilators - Reduce bronchial inflammation - Reduce bronchial hyper-reactivity to stimuli - Have delayed onset of action (effect usually attained after 2-4 weeks). - Maximum action at 9-12 months. - Given as prophylactic medications (as prophylactic therapy to reduce frequency of asthma attacks). - Effective in allergic, exercise, antigen and irritant-induced asthma. - Abrupt stop of corticosteroids should be avoided and dose should be tapered (adrenal insufficiency syndrome). 	<p style="text-align: center;">Uses</p> <p>Inhalation:</p> <ul style="list-style-type: none"> - relatively safe - As a prophylactic therapy to control moderate to severe asthma in children and adults alone or in combination with beta-agonists. - Upregulate β_2 receptors (have additive effect to B2 agonists). <p>Systemic corticosteroids are reserved for:</p> <ul style="list-style-type: none"> - management of acutely ill patients. - Status asthmaticus (i.v.). 	<p style="text-align: center;">Side Effects</p> <p>2- In systemic prolonged oral + parenteral uses:</p> <ul style="list-style-type: none"> - Adrenal suppression - Growth retardation in children – Osteoporosis - Fat distribution - Hypertension – Hyperglycemia – Fluid retention. - Weight gain - Susceptibility to infections - Cataract - Glaucoma - Wasting of the muscles - Psychosis <p>1- Inhalation has very less side effects:</p> <ul style="list-style-type: none"> - Oropharyngeal candidiasis (thrush). - Dysphonia (voice hoarseness).

Name of the group	Pharmacokinetics	Pharmacodynamics	
2- Mast cell stabilizers.	<ul style="list-style-type: none"> - Inhalation (aerosol, microfine powder, nebulizer). - Poor oral absorption (10%) - half life is 90 minutes. 	<ul style="list-style-type: none"> - Not direct bronchodilators - Not effective in acute attack of asthma. - Prophylactic anti-inflammatory drug - Reduce bronchial hyper-reactivity. - Effective in exercise, antigen and irritant-induced asthma. - Children respond better than adults 	
	Uses	Side effects	e.g
	<ul style="list-style-type: none"> - Prophylaxis in asthma especially in children. - Allergic rhinitis. - Conjunctivitis 	<ul style="list-style-type: none"> • Bitter taste • minor upper respiratory tract irritation (burning sensation, nasal congestion) <p>If someone come with upper respiratory tract the mast cell stabilizers will not effect that much .</p>	Cromolyn (Sodium cromoglycate) - Nedocromil act partially by stabilization of mast cell membrane.

Leukotrienes

- Synthesized by inflammatory cells found in the airways (eosinophils, macrophages, mast cells).
- Products of 5-lipo-oxygenase on arachidonic acid.

Leukotriene B4:

chemotaxis of neutrophils

Cysteinyl leukotrienes C4, D4 & E4:

- bronchoconstriction
- increase bronchial hyper-reactivity
- mucosal edema
- mucus hyper-secretion

Leukotrienes antagonists The drugs from this group may : 1- 5-lipoxygenase inhibitor (Zileuton) 2-leukotriene-receptor antaonists (Zafirlukast)	Zileuton :selective inhibitor of 5-lipo-oxygenase Give orally Because it has short duration it is given 3-4 times per day	Zafirlukast : selective , inhibit cysteinyl leukotriene receptors (LTD4)
	Uses: Bronchodilator Anti-inflammation Less effective than corticoste Potentiate corticosteroid . Prophylaxis of mild to moderate asthma	Side effects: Increase liver enzyme Headache Dyspepsia Rare:churg-strauss syndrome (eosinophilic vasculitis)

Omalizumab : antibody directed against human IgE

Any drug ends with "mab" that means it is antibody.