

drugs of bronchial asthma

Bronchial asthma...

- Acute asthma
- Chronic asthma
- Status asthmaticus (acute severe asthma)

types

Bronchial asthma

- Impairment of airflow due to constriction of bronchial smooth muscle (bronchospasm)
- Swelling of bronchial mucus secretion.

Factors:

- Allergy, infection, psychological factors,
- Air way obstruction may be due to release of the mediators from sensitized mast cells in the lungs.

Mediators of bronchial asthma...

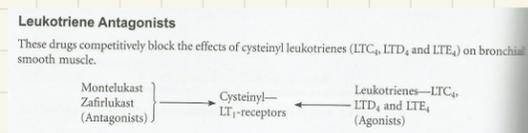
- Histamine
- 5-HT (serotonin)
- Prostaglandins
- Leukotriens (LTC₄ and LTD₄)
- Protease
- Platelet activation factor (PAF)
- Bronchial asthma may be episodic or chronic.

- β_2 blockers
- Cholinomimetics
- cold weather
- exercise

Classification of antiasthmatic drugs

Leukotriene Receptor antagonist

- ↳ Zafirlukast
- ↳ Montelukast



These drugs competitively blocks the effects of cysteinyl leukotrienes (LTC₄, LTD₄, LTE₄) on bronchial smooth muscle.

Produce bronchodilation.

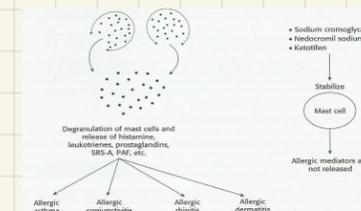
- Suppress bronchial inflammation
- Decrease hyper-reactivity
- Well absorbed after oral administration.
- Highly bound to plasma protein.
- Effective in prophylactic treatment of mild asthma.
- Well tolerated and has less side effects.

Anti-Ig-E antibody

- ↳ Omalizumab

- prevents binding of IgE to mast cell, thus prevent mast cell de-granulation.
- It has no effects on IgE already bound to mast cells.
- Administered parenterally.
- Used in moderate to severe asthma and allergic disorders such as nasal allergy, food allergy, etc. approved for use in patient above 12 years of age.

Mast cell stabilizers



- They are not bronchodilators.
- Inhibits release of various mediators-histamine, LTs, PGs PAF etc.
- Stabilizes the mast cell membrane.

Sodium chromoglycate

- not effective orally / poorly absorbed from gut.
- given by inhalation route.

- Uses :-
- As prophylactic agent to prevent bronchospasm induced by allergens and irritants.
 - Can be used in allergic conjunctivitis, allergic rhinitis, allergic dermatitis, etc.
 - Used by topical route as prophylactic agent.

Glucocorticoids

Systemic

- ↳ hydrocortisone iv
- ↳ prednisolone
- ↳ methylprednisolone

Inhalational.

- ↳ beclomethasone
- ↳ budesonide
- ↳ fluticasone

- Glucocorticoids secrete lipocortin which inhibits phospholipase A2 and thereby prevent formation of various mediators such as PGs, TXA2 etc.
- Have anti-allergic, anti-inflammatory and immunosuppressant effects.

- Suppress inflammatory response to Ag: Ab reaction.
- Decrease mucosal oedema.
- Reduced bronchial hyperreactivity.
- Do not have direct bronchodilating effect but potentiates the effects of β -adrenergic agonists
- They are well tolerated.

* Combination of long acting β -agonists (LABA) with steroid is available

- ↳ fluticasone + salmeterol
- ↳ budesonide + formoterol

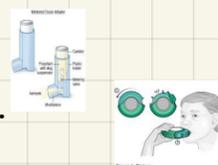
→ synergistic action
in COPD & bronchial asthma

Adverse effects

- gastric irritation, Na⁺ and water retention, hypertension, muscle weakness, osteoporosis, HPA-axis suppression etc.

Inhalational devices

- Metered dose inhaler (MDI)- used with spacer device.
- Dry powder inhalers- spinhaler and rotahaler
- Nebulizers- useful in acute severe asthma, COPD, and children



Treatment of acute severe asthma

- Humidified oxygen
- Nebulized β_2 -adrenergic agonist (salbutamol 5 mg/terbutaline 10 mg) + anticholinergic agents (ipratropium bromide 0.5 mg).
- Systemic glucocorticoids: i.v. hydrocortisone 200 mg stat followed by 30-60 mg prednisolone/day.
- I.V. fluid to correct dehydration.
- K⁺ and sodium bicarbonates supplements.
- Antibiotics

Bronchodilators

Bronchodilators
Sympathomimetics (see p. 84)
Mechanism of action

Sympathomimetics \oplus β_2 \rightarrow \uparrow cAMP \rightarrow

- Bronchodilatation
- Inhibit the release of histamine, SRS-A (LTC_4 and LTD_4) from mast cells
- Promote mucociliary clearance

Act by stimulating β_2 -receptors in the bronchial smooth muscle and mast cells

- The first line drugs for bronchial asthma.
- Well tolerated when inhaled.
- At high doses may cause tremor, tachycardia, palpitation, hypokalaemia.

Anticholinergics

- ↳ Ipratropium bromide } atropine substitutes
- ↳ tiotropium bromide }

- Selectively blocks the effects of ACh in bronchial smooth muscle and cause bronchodilation.
- Slow onset of action and are less effective.
- These drugs are preferred in COPD.
- Administered by inhalation route.
- Combination with β_2 -adrenergic agonist have better effects.

passive bronchodilation.
 so

Sympathomimetics

Selective β_2 -adrenergic agonist

Non-selective
 ↳ adrenaline

- ↳ Terbutaline (short acting)
- ↳ salmeterol
- ↳ salbutamol
- ↳ Formoterol (long acting)

- produce prompt and powerful bronchodilation by acting through β_2 adrenergic receptors.
- Useful in acute attack of asthma (0.2-0.5 ml of 1:1000 solution given s.c.)
- Its use decline due to serious cardiac side effects.

Salbutamol and terbutaline	Salmeterol	Formoterol
Selective β_2-agonists: On inhalation, they have a rapid onset (within 1-5 minutes) and short duration of action. They are preferred for acute attack of asthma. Route and dose: Inhalation, salbutamol 100-200 mcg every 6 hours, or as and when required through metered dose inhaler (MDI) to terminate an acute attack. Other routes of administration are oral, i.m. and i.v.	Long-acting selective β_2-agonist: It is preferred for maintenance therapy of asthma. It is not suitable for acute attack as it has a slow onset of action. Route and dose: Inhalation, 50 mcg twice daily	Long-acting selective β_2-agonist: It has a rapid onset of action. It is preferred for prophylaxis due to long duration of action. Route and dose: Inhalation, 12-24 mcg twice daily

Drugs to be avoided in asthma

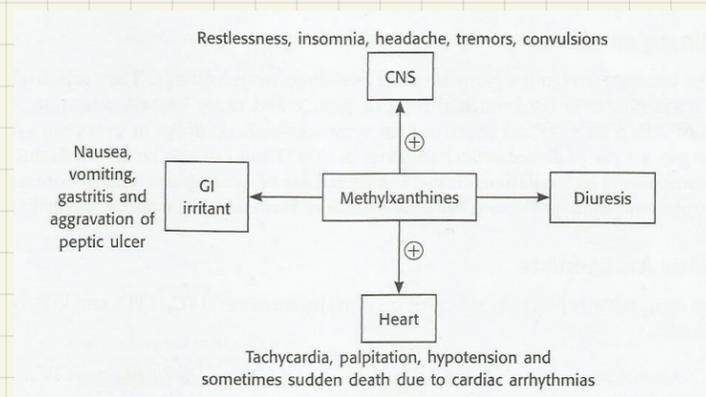
- NSAIDs
- β -adrenergic blockers.
- Cholinergic agents

Methylxanthine

- ↳ theophylline → poorly water soluble, hence not suitable for injection, available for oral administration.
- ↳ aminophylline → water soluble but highly irritant. Administered orally or slow i.v.
- ↳ etophylline → given by oral, i.m., i.v. routes.

Adverse effects:

have narrow margin of safety, tachycardia, palpitation, hypotension, death due to cardiac arrhythmias.



Mechanism of action of methylxanthines

- Theophylline } Inhibit phosphodiesterase (PDE) \rightarrow \uparrow cAMP \rightarrow
 - Aminophylline }
- Bronchodilatation
 - Inhibit the release of histamine and SRS-A from mast cells
 - Improve mucociliary clearance in respiratory passages

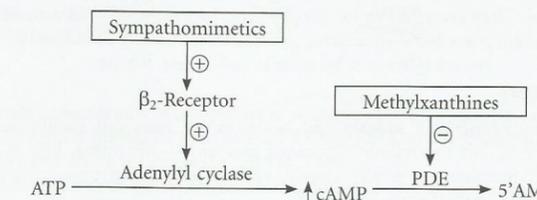
- Their uses are markedly reduced due to their narrow therapeutic index and available of better antiasthmatic drugs.
- Methylxanthine are third or fourth line drugs in the treatment of asthma.
- Methylxanthines are well absorbed after oral and parenteral administration.
- Food delays the rate of absorption of theophylline, well distributed, cross placenta & BBB, metabolised in liver and excreted in urine.

Drug interactions

- Phenytoin/ rifampicin/phenobarbitone x theophylline
- Cimetidine/ciprofloxacin/erythromycin x theophylline.

Drug interactions

1. Sympathomimetics \times Methylxanthines



Uses:

- Bronchial asthma and COPD
- Premature apnoea in infants