

PHARMACOTHERAPY OF BRONCHIAL ASTHMA

Dr. Shrinivas R Raikar
Asst. Professor
Pharmacology

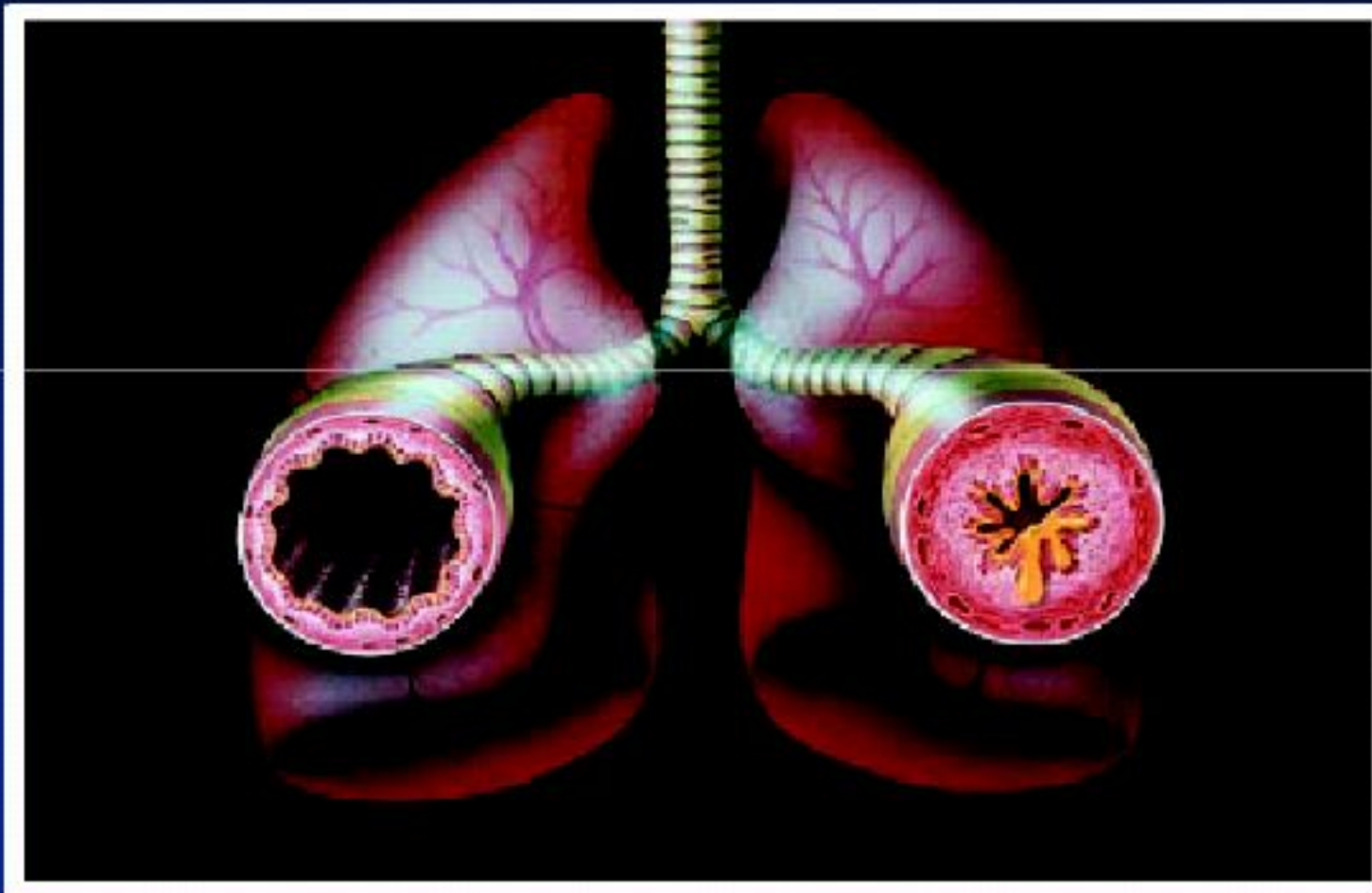
Contents

- Definition
- Drug classification
- Individual drugs and mechanism of action
- Choice of treatment
- Aerosol drug delivery
- Drugs to be avoided
- Conclusion

Asthma is a **chronic inflammatory** disorder of the airways.

1. Hyper responsiveness
2. Broncho-constriction
3. Mucus plugs
4. Reversible airway obstruction

Representation of Airways in Normal Lung and in Asthma



Drugs used in Bronchial Asthma

1. Bronchodilators

- Sympathomimetics - β 2 agonists
- Anticholinergics - **Ipratropium**, Tiotropium
- methylxanthines - **Theophylline**, **Aminophylline**

2. Anti-inflammatory agents

1. Corticosteroids
2. Mast Cell Stabilizers
3. Leukotriene Modulators
4. Monoclonal Anti-IgE Antibody - Omalizumab

Drugs used in Bronchial Asthma

Bronchodilators

1. Selective β 2- Agonists

Short acting

- Salbutamol**
- Terbutaline**
- Remiterol**
- Fenoterol**

Long-acting

- Salmeterol,**
- Formoterol,**
- Bambuterol.**

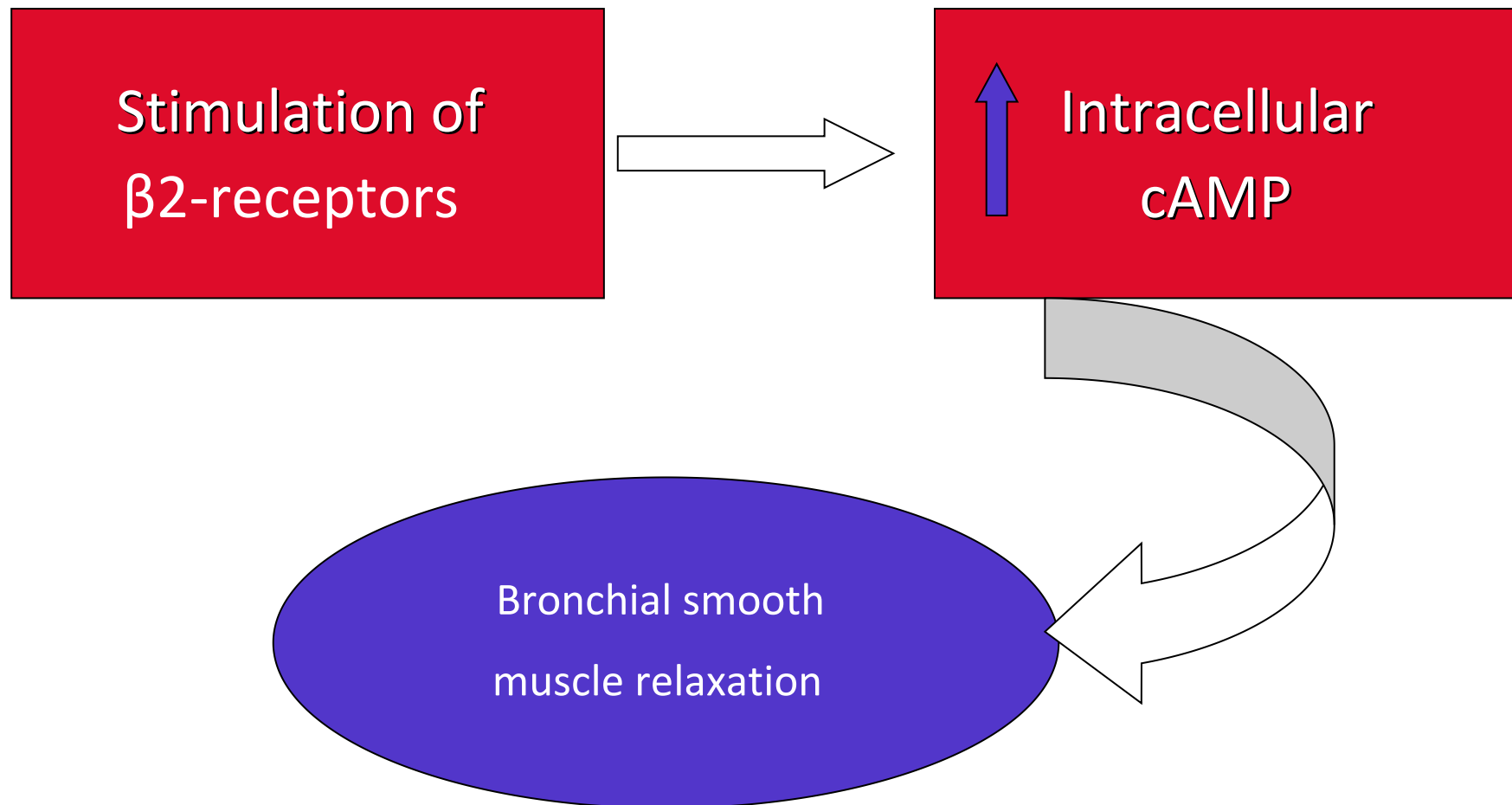
2. Non-selective Sympathomimetics

- Adrenaline
- Ephedrine,
- Isoprenaline.

1. β 2-Selective adrenoceptor agonist

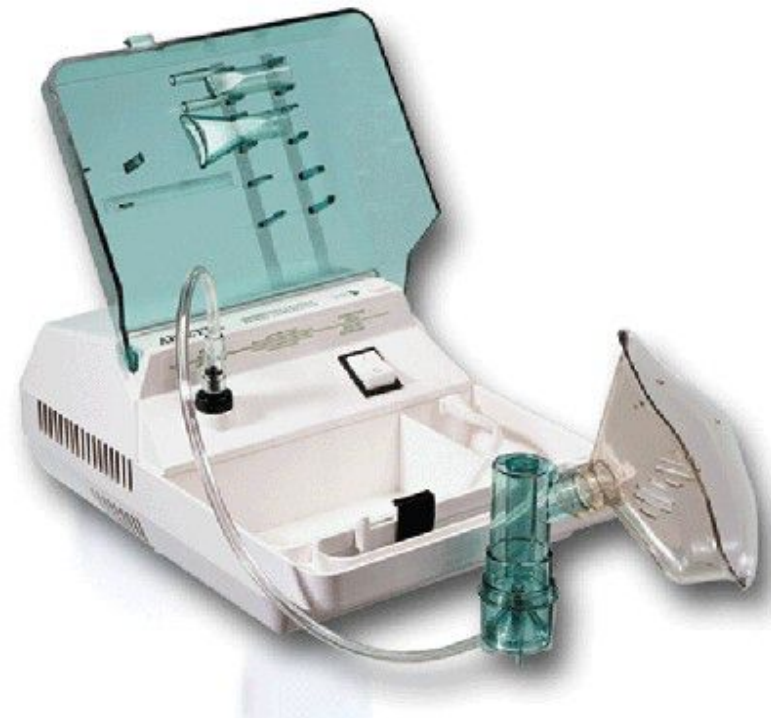
- most widely used drugs .
- 1. Short acting:- Salbutamol, Terbutaline
used only for acute attack
- 1. Long acting:- Salmeterol, Formeterol
used for only prophylaxis

β 2 receptor agonist-mechanism of action



Selective β_2 receptor agonists

1. Route of administration:
 - Usually delivered via a metered dose inhaler with immediate effect
 - i.v used for acute attack.
 - S.C. (terbutaline)
 - Nebulization



Selective β 2 receptor agonists

2. Adverse effect:

- Cardiac arrhythmias (at high dose has β 1 effects)
- Tolerance to β agonist action.
- Skeletal muscle tremors.

Non-selective Sympathomimetics

Adrenaline/epinephrine:

- ✓ Agonist of α and β receptor
- ✓ Adverse effect of cardiovascular system like Tachycardia, Hypertension, Worsening of angina and even arrhythmias.
- ✓ less used
- ✓ S.C. injection(0.5 ml of 1:1000 adrenaline)

Muscarinic antagonist - ipratropium



- ❖ Quaternary derivative of atropine
- ❖ Act by competitive blocking of muscarinic receptors (M3 subtype) in bronchioles
- ❖ Also decrease mucus gland secretion
- ❖ Reverses acute bronchospasm and vagally mediated bronchospasm
- ❖ Ineffective in allergen or exercise induced asthma

Ipratropium bromide - use

- Alternative in patients with β 2 agonist allergy
- DOC for bronchospasm due to β blocker medication.
- Adjunct in moderate to severe asthma

Dose

MDI – 18mcg/puff; 2-4 puffs every 6 hour

Route of administration: Metered dose inhalers



Tiotropium bromide



- Long acting (action last 24 hours)
- Patients of asthmatic bronchitis, COPD and psychogenic asthma

Theophylline

Mechanism of action :

1. Inhibit activity of PDE \longrightarrow cAMP[↑] \longrightarrow bronchial relaxation

2. cAMP $\xrightarrow{\text{PDE}}$ 5AMP

3. Inhibition of the cell surface receptor of adenosine

Theophylline



- ❖ Metabolised by P450 enzyme system
- ❖ Microsomal enzyme inhibitor

Route of administration: Orally(200mg, 300mg TDS)

Theophylline:



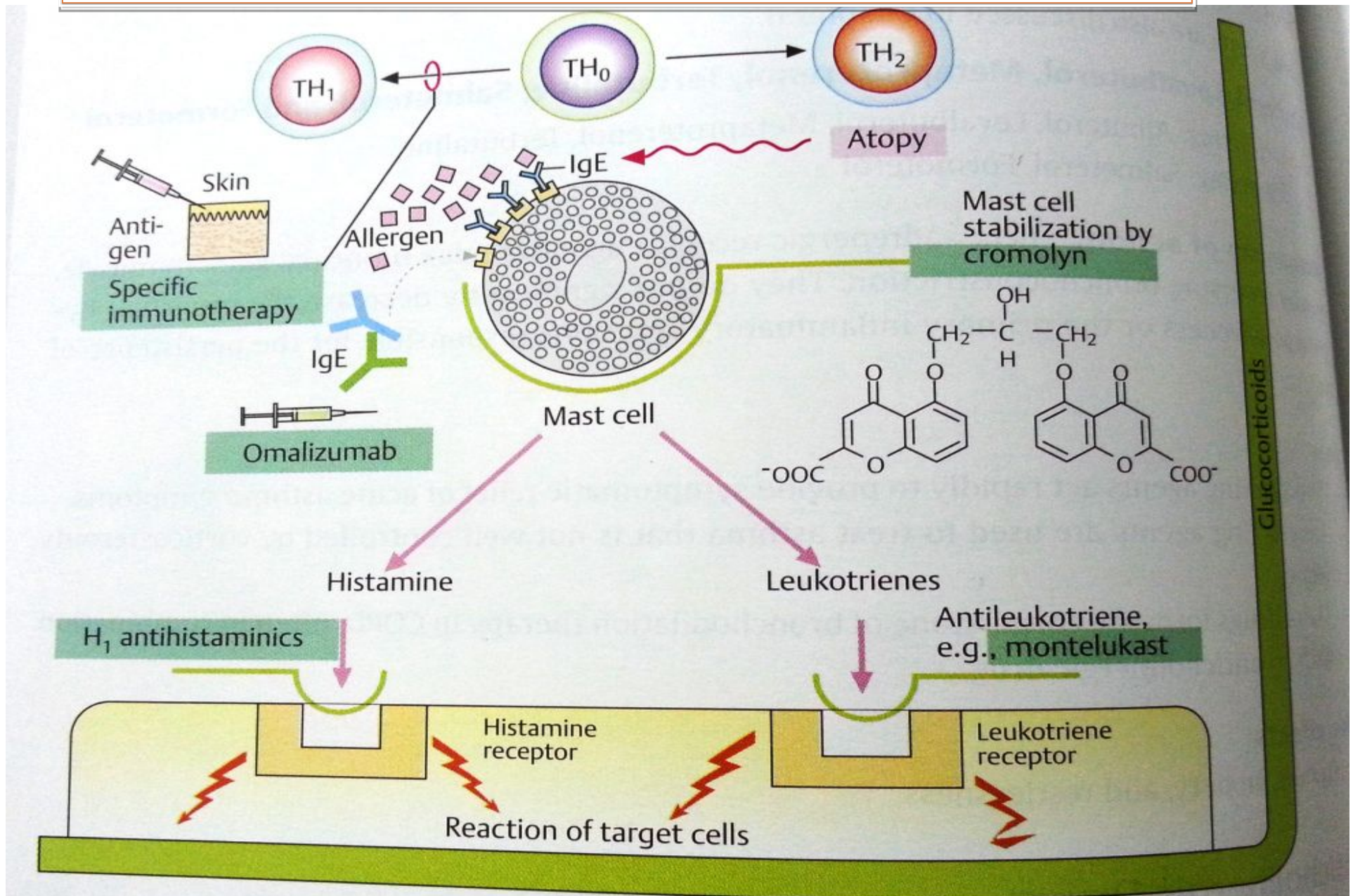
Adverse effects

- It has a narrow therapeutic index
- Its therapeutic and toxic effects are related to its plasma concentration.
- <20mg/L: Nausea, vomiting, headache, anxiety, abdominal discomfort.
- 20-40mg/L: Arrhythmia



Anti-inflammatory drugs

Targets of anti-inflammatory drugs



Glucocorticoids

- Mechanism:
 1. Depress the inflammatory response in bronchial mucosa thus diminish bronchial hyperresponsiveness.
 2. Anti-inflammatory effect (inhibit phospholypaseA2)
 3. Immunosuppressive effect.

Glucocorticoids -Route of administration

1. Inhalational

- ❑ Metered dose inhaler: (deeply & slowly inhale)
- ❑ Budesonide 200 to 400 µg BD or QID
- ❑ Beclomethasone 50µg or 100µg per meter dose

2. Systemic

- ❑ Intravenous used for: severe asthma, status asthmaticus (hydrocortisone 100 mg 8th hourly)
- ❑ oral- prednisolone (10mg BD)

Inhalational steroids – side effects



Local

- ⊙ Cough
- ⊙ Dysphonia
- ⊙ Oral candidiasis
- ⊙ Minimised by using inhalation chamber and mouth washing

SYSTEMIC

- ⊙ May occur with high dose therapy
- ⊙ Adrenal suppression, osteoporosis etc.

Mast cell stabilizers



- Drugs

- ⊙ **Sodium Cromoglycate, Nedocromil, Ketotifen**

- Modulate mast cell mediator release
- Decrease eosinophil recruitment
- Inhibit both early and late responses to allergen challenge and exercise induced asthma

Mast cell stabilizers



Dose and route

- ⦿ Cromolyn – 800mcg per puff (2-4 puffs 4 times a day)
- ⦿ Ketotifen (oral dose 1 to 2 mg BD)

USE

- Long term control medications that prevent asthma symptoms
- Improve air way function in mild persistent asthma
- May help to reduce the dose of steroids

Leukotriene modifiers



Drugs :

- ⦿ **5-Lipoxygenase inhibitor: Zileuton**

Mechanism :

- ⦿ Block leukotriene production
- ⦿ Block lipo-oxygenase enzyme

Use :

- Alternatives to low dose steroids in mild persistent asthma

Leukotriene modifiers



Drugs

- ⦿ **LT-receptor Antagonists: Zafirlukast, Montelukast.**

Mechanism

- ⦿ Block receptors LT₁ receptors and block the effects of LTC₄, LTD₄, and LTE₄.

Use

- Alternatives to low dose steroids in mild persistent asthma for prophylaxis
- Allergic rhinitis

dose and Adverse effects



- Zileuton - 600mg QID
 - ⊙ reversible elevation of aminotransferases
- Montelukast - 10mg OD in evening
- A/E
 - ⊙ Churgstrass syndrome

Monoclonal anti IgE antibody



Omalizumab

Mechanism of action:

- Prevents the binding of IgE to mast cell & thus prevents mast cell degranulation

Rout of administration:

- i.v or s.c

Side effects:

- Redness, stinging, itching, induration.

Choice of treatment



1. Mild episodic asthma

Inhaled short-acting beta2 agonist at onset of each episode

2. Seasonal asthma

start regular inhaled cromoglycate/low dose

inhaled steroid(200-400µg/day) 3-4 wks before

anticipated seasonal attacks continue till 3-4 wks

after the season is over treat individual episodes

with inhaled short acting β 2 agonist.



3. Mild chronic asthma with occasional exacerbations:

regular inhaled sodium cromoglycate, short acting β 2 agonist(step-2)

4. Moderate asthma with frequent exacerbations:

increase doses of steroid (up to 800 μ g/day) +inhaled long acting β 2 agonist(step-3)



5. Severe asthma:

Regular high dose inhaled (steroids 800-2000 μ g/day)

though a large volume spacer device + inhaled long-

acting β_2 agonist (salmeterol) twice daily .



6. Status asthmaticus

- Any pt of asthma has the potential to develop acute severe asthma which may be life threatening.
- upper respiratory tract infection is the most common precipitant.

Status asthmaticus



- Acute severe exacerbation of asthma characterized by
 - ⊙ Severe limitation of airflow
 - ⊙ Increased work of breathing
 - ⊙ Hypoxia (low tissue pO₂)

Management of status asthmaticus




- ❑ Hydrocortisone hemisuccinate 100mg I.V stat followed by 100-200mg 4-8 hourly infusion
- ❑ Nebulized salbutamol (2.5-5mg)+ipratropium bromide (0.5mg) intermittent inhalations driven by O₂.

Management of status asthmaticus



- ❑ High flow humidified oxygen inhalation.
- ❑ Salbutamol/terbutaline 0.4mg i.m/s.c may be added,
since inhaled drug may not reach smaller bronchi due to
severe narrowing/plugging.
- ❑ Intubation & mechanical ventilation, if needed.

- 
- ❑ Treat chest infection with intensive antibiotic therapy.
 - ❑ Correct dehydration and acidosis with saline+sod.
bicarbonate/lactate infusion.

Aerosol Delivery of Drugs

- High local concentration in bronchioles
- Low systemic side effect.
- Increased bioavailability.
- Optimal particle size for deposition in small airways – 1 to 5 μm



Aerosol Delivery Devices:



Liquid aerosols

- Metered dose inhaler (MDI)
- Nebulizer

Powdered drugs

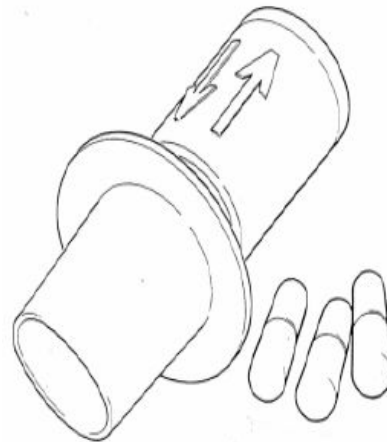
- Dry powder inhaler (DPI), Spinhaler, Rotahaler

PMDI

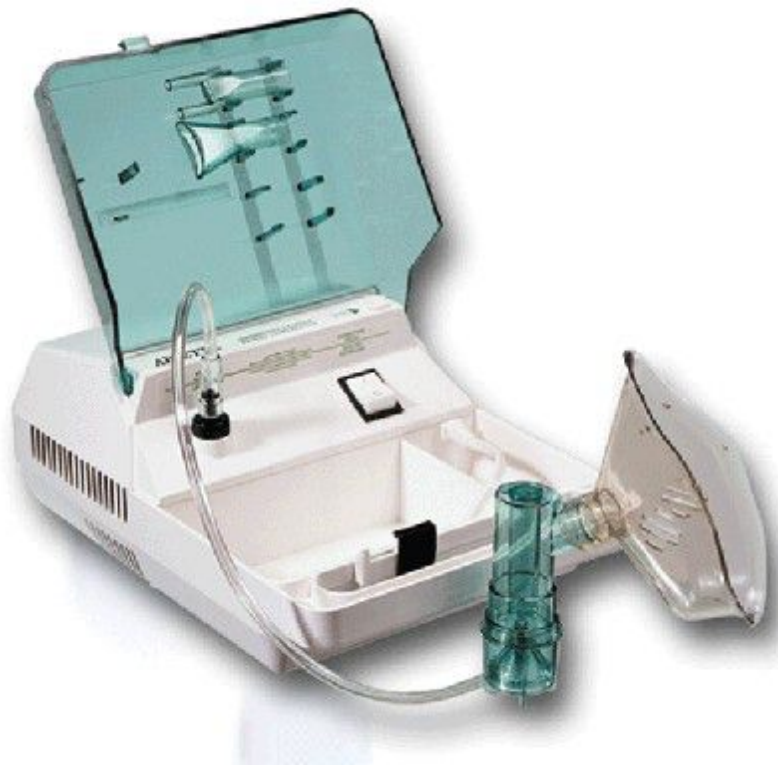


Rotacap

SPACER



NEBULIZER



DPI(Dry powder inhaler)



Drugs to be avoided in patient with bronchial asthma



1. NSAIDS like aspirin, ibuprofen, diclofenac etc. (paracetamol can be used)
2. Non selective Beta-adrenergic blockers
3. Cholinergic agents.

Conclusion



- Asthma is treated with two types of medicines:
 - ⦿ Long term control - to reduce airway inflammation and prevent asthma symptoms.
 - ⦿ Quick-relief medicines relieve asthma symptoms that may flare up.
- Initial treatment will depend on severity of the disease.



Thank You

