

MECHANISM OF ANTI-ASTHMATICS

1. BRONCHODILATORS-

- I. SYMPATHOMIMETICS-Adrenergic drugs cause bronchodilatation through β_2 receptor stimulation \rightarrow increased cAMP formation in bronchial muscle cell \rightarrow relaxation. In addition, increased cAMP in mast cells and other inflammatory cells decreases mediator release. Since β_2 receptors on inflammatory cells desensitize quickly, the contribution of this action to the beneficial effect of β_2 agonists in asthma where airway inflammation is chronic, is uncertain, and at best minimal. Adrenergic drug is the mainstay of treatment of reversible airway obstruction, but should be used cautiously in hypertensives, ischemic heart disease patients and in those receiving digitalis. They are the most effective and fastest acting bronchodilators when inhaled.

Sub classes of sympathomimetic –

- Alpha- beta receptors agonist
- Non selective beta agonist
- Selective beta 2agonist – These are divided into 2 classes
 - Short acting – eg. Salbutamol, Terbutaline
 - Long acting – eg. Bambuterol, Salmeterol, Formoterol

METHYLYXANTHINES- Three distinct cellularactions of methylxanthines have been defined—

- Release of Ca^{2+} from sarcoplasmic reticulum, especially in skeletal and cardiac muscle
- **Inhibition of phosphodiesterases:** Phosphodiesterases which degrades cyclic nucleotides intracellularly are blocked by theophylline
Bronchodilation occur due increased cAMP

- **Blockade of adenosine receptors:** Theophylline combines with the adenosine receptors and blocks its regular bronchodilation

ANTICHOLINERGICS -Antimuscarinic drugs cause bronchodilation by blocking M₃ receptor mediated cholinergic constrictor tone; act primarily in the larger airways which receive vagal innervation. However, some recent evidence points to presence of M₃ receptors on peripheral bronchiolar muscles as well, though they are not vagally innervated. anticholinergics. They are the bronchodilators of choice in COPD. Reflex cholinergic tone appears to be the major reversible component of airway obstruction in COPD.

Leukotriene modifiers - The cysteinyl leukotrienes (LT-C₄/D₄/E₄) are important mediators of bronchial asthma. Two cysteinyl leukotrienes receptor antagonist (**montelukast, zafirlukast**), and **5-LOX inhibitors (zileuton)** are recently available. The half-life of montelukast is 3-6 hrs, while that of zafirlukast is 8-12 hrs. Dose-10 mg OD

GLUCOCORTICOIDS -Glucocorticoids are not bronchodilators. They benefit by reducing bronchial hyperreactivity, mucosal edema and by suppressing inflammatory response to AG:AB reaction or other trigger stimuli.

Systemic steroid therapy is resorted to in asthma under the following two situations:

- (i) **Severe chronic asthma:** not controlled by bronchodilators and inhaled steroids, or when there are frequent recurrences of increasing severity; start with prednisolone 20–60 mg (or equivalent) daily; attempt dose reduction after 1–2 weeks of good control and finally try shifting the patient onto an inhaled steroid. Only few patients require long term oral steroids—in them dose should be kept at minimum. In patients requiring long-term

glucocorticoid therapy, alternative treatment with immunosuppressants like methotrexate (low dose) or cyclosporine has been tried.

(ii) *Status asthmaticus/acute asthma exacerbation:*

Asthma attack not responding to intensive bronchodilator therapy: start with high dose of a rapidly acting i.v. glucocorticoid which generally acts in 6–24 hours— shift to oral therapy for 5–7 days and then discontinue abruptly or taper rapidly.

Inhalation- These are glucocorticoids with high topical and low systemic activity (due to poor absorption and/or marked first pass metabolism). *Beclomethasone dipropionate*, *Budesonide* and *Fluticasone* have similar properties. *Ciclesonide* is a later addition. Because airway inflammation is present in early

IMMUNOSUPPRESSANT AGENTS- Which used in severe patient or steroids dependent asthma

Examples: Cyclosporine, methotrexant, Gold compound

MISCELLANEOUS-

- Selective anti IgE antibody
- Calcium channel blocker
- Smooth muscle dilation
- Anti-histaminics