**Pharmacology of respiratory system**

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**The main symptoms of respiratory diseases are:-**

A-Cough

B-Dyspnea

C-Nasal congestion

**A-TREATMENT OF COUGH**

1-We must exclude any drugs used by the patients which causing cough like ACE INHIBITORS.

2- Cough reflex is via both the afferent and efferent nerves (i.e. involving the central and peripheral nervous systems), as well as the smooth muscles of the bronchial tree.

3- A useful physiological mechanism that serves to clear the respiratory tract of foreign materials and excess secretions.

It should not be suppressed indiscriminately. However, cough at times may not serve any useful/ physiological purpose and could therefore be pathologic

\* Productive cough should not be suppressed as sputum needs to be cleared.

***Drugs:***

***I. Antitussives:***

**Centrally-acting Antitussives**

**a**. Narcotics:

Opiates: Codeine, Pholcodeine, Hydrocodone, Morphine.

Opioid derivatives: Dextromethorphan, Levopropozyphene, Noscapine

**b**. Non-Narcotics: Benzonatate, first generation Antihistamines e.g. Diphenhydramine, having sedative, anticholinergic actions, crossing the BBB

**II. Expectorants (Mucokinetics**

Make cough more productive by loosening and liquefying bronchial secretions.

Reflexly-acting

a. Ipecacuanha

b. Ammonium chloride

c. Potassium iodide

Directly-acting:

Guaiphenesin

**III. Mucolytics**

Break down thick mucus, making it thinner and easier to cough out. Split disulphide bonds in mucoprotein present in sputum and reduces its viscosity.

Acetylcysteine

Carbocysteine

Methylcysteine

**IV. Demulcents**

E.g. Liquorice, Glycerin, Lozenges.

They provide relief to throat

Promote salivation and inhibit impulses from inflamed mucosa

***TREATMENT OF DYSPNIA***

Dyspnea is the non-desire sign bronchoconstriction as in ASTHMA AND COPDs

Lower respiratory tract disorders include infections, restrictive pulmonary disorders, obstructive pulmonary disorders, and lung cancer

**Lower Respiratory Tract Infections**

1. 1-Acute Bronchitis: An infection that is located in the bronchi is called bronchitis. Most of the time, it is preceded by a viral URI that led to a secondary bacterial infection. Usually, a nonproductive cough turns into a deep cough that will expectorate mucus and sometimes pus.

2-Asthma

3. Chronic Obstructive Pulmonary Disease

\*Cough - this is the most common symptom and is usually dry and persistent. Coughing can occur any time, but it is often worsened at night and after exercise.

Wheezing - a high-pitched wind blowing noise, usually heard on breathing out.

Shortness of breath - breathing is fast and shallow. Unable to get enough air into the lungs.

Chest Tightness - The chest feels ‘tight’ and unable to expand freely when breathing.

. Asthma may be acute or chronic.

-**Chronic asthma**: individual has intermittent attacks of dyspnoea, wheezing and cough.\*

-**a**

**Acute severe asthma (status asthmaticus):** not easily reversed. Often fatal and requires prompt and aggressive treatment. Hospitalization is necessary.

Asthma may be intrinsic or extrinsic.

-Intrinsic (Type II, Non-allergic reaction): no obvious allergic basis. Cold, respiratory tract infection, changes in weather, exercise, stress, etc. are precipitating factors and may induce inflammatory reactions. It predominates in small children particularly below 5 years and in adults over the age of 45 years

The treatment aims to reverse airflow obstruction and reduces asthma exacerbations thus improving quality of life. However, long-term use of high dose inhaled corticosteroids therapy may lead to detrimental effects, such as cataracts, osteoporosis in elderly patients, and stunting of growth in children.

Moreover, the combination therapy may not modify the disease progression and are not curative

**\*Medications include quick-relief therapies to treat acute symptoms of an attack and long-term control medications to prevent further exacerbations*.***

.**1-Bronchodilators**-sympathomimetics, methylxanthines, anticholinergics

**2-Corticosteroids**-systemic, inhalation

Leukotriene antagonists. **3-Mediator -antagonists:** Antihistamine

. **Mast cell stablizers**  **4-**

**. 5-Anti-IgE antibody**

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**\*BRONCHODILATORS**

Are medications that relax the bronchial muscles, making the airway larger, and allowing air to pass through easily

Thus relieving breathlessness, chest tightness, and other acute symptoms of asthma

.Sympathomimetics-β2-receptor agonists1-

i. Short-acting: salbutamol, pirbuterol, terbutaline

ii. Long-acting: salmeterol, formoterol

**Salbutamol**: **1**

**Mechanism**- Beta adrenoceptors are coupled to a stimulatory G protein, which activates adenylyl cyclase to produce the second messenger cAMP

In the lung, cAMP decreases Ca++ concentrations within the cells and activate myosin light chain phosphatase.

In addition, there is increased membrane potassium conductance.

All these culminate into muscle relaxation

**Side effects**

Nervousness, restlessness, tremor, headache, insomnia, chest pain, palpitations, angina, hypertension, tachycardia

Xanthine derivatives:

Theophylline:

Water insoluble

Theophylline + Ethylene Di-Amine = Aminophylline

**Mechanism:** Theophylline is a competitive nonselective phosphodiesterase inhibitor, which raises intracellular cAMP, activates Protein kinase A, inhibits TNF- alpha and inhibits leukotriene synthesis, and reduces inflammation and innate immunity.

Nonselective adenosine receptor antagonist. (Adenosine is a bronchoconstriction)

* **Pharmacological effects**
* Bronchial muscle: Bronchodilatation
* CNS: cortical stimulation, excitement, insomnia, stimulation of medullary respiratory and vomiting centre, reduced mental exhaustion and fatigue.

**Side effects of theophylline**

Nausea, vomiting, convulsion, arrhythmias, anorexia, palpitations

**Therapeutic index is very low**

**Indications:-**

Bronchial asthma

COPD

Apnea

***Anticholinergic drugs***

Short-acting: ipratropium

Long-acting: tiotropium

Anticholinergics prevent the increases in intracellular concentration of cyclic guanosine monophosphate (cyclic GMP), most likely, due to actions of cGMP on intracellular calcium, this results in decreased contractility of smooth muscle in the lung, inhibiting bronchoconstriction and mucous secretion.

***Corticosteroids***

. Topical inhalation:1

- betamethasone

- beclomethasone

. Systemic: 2

- oral prednisolone

- i.v: hydrocortisone

Methyl prednisolone (Depomedrol) as injection

**Mechanisms of Action**:

Inhibit the formation of cytokines1

2 Inhibit the generation of vasodilators PGE2 and PGI2 by inhibiting the induction of cyclooxygenase 2.

3 Induce lipocortin (a phospholipase A2 inhibitor) therefore, inhibiting LTC4 and LTD4 production.

4. Decrease the synthesis of leucocyte chemotaxins LTB4 and PAF, thus reducing recruitment and activation of inflammatory cells.

5. Inhibition of synthesis of bronchoconstrictor substances e.g. histamine

6 Suppression of enzymatic processes that are triggered by the union of antigen with antibody.

7 Reduces antibody formation

**Side effects of corticosteroids**

Adrenal suppression

Impairment of wound healing

Peptic ulcer

Immunosuppression

Osteoporosis

Hyperglycemia

Menstrual irregularities

Fluid retention

Muscle weakness.

**Prophylactic agents in BA:**

**1 -Mast-cell stabilizers**

i. Cromones: - Na cromoglycate, Nedocromil Na

ii. Ketotifen

**Mechanism of Action**

Inhibit release of mediators from mast cells by stabilizing the mast cells.

Inhibit several inflammatory cells e.g. neutrophils, macrophages, eosinophils. Cromoglycate is poorly absorbed from the gut, so it is only effective through inhalation.

Ketotifen: is both a 5HT and histamine antagonist. Orally active but with a slow onset of action. Must be administered regularly for 6-12 weeks before any beneficial effect is noticeable.

**2 -Mediator Antagonists**

i. Antihistamines: azelastine, cetirizine

ii. Leukotriene pathway inhibitors:

-lipoxygenase enzyme inhibitor: zileuton

- leukotriene-receptor antagonists: zafirlukast, montelukast, pranlukast

**The End…… (Thank you)**