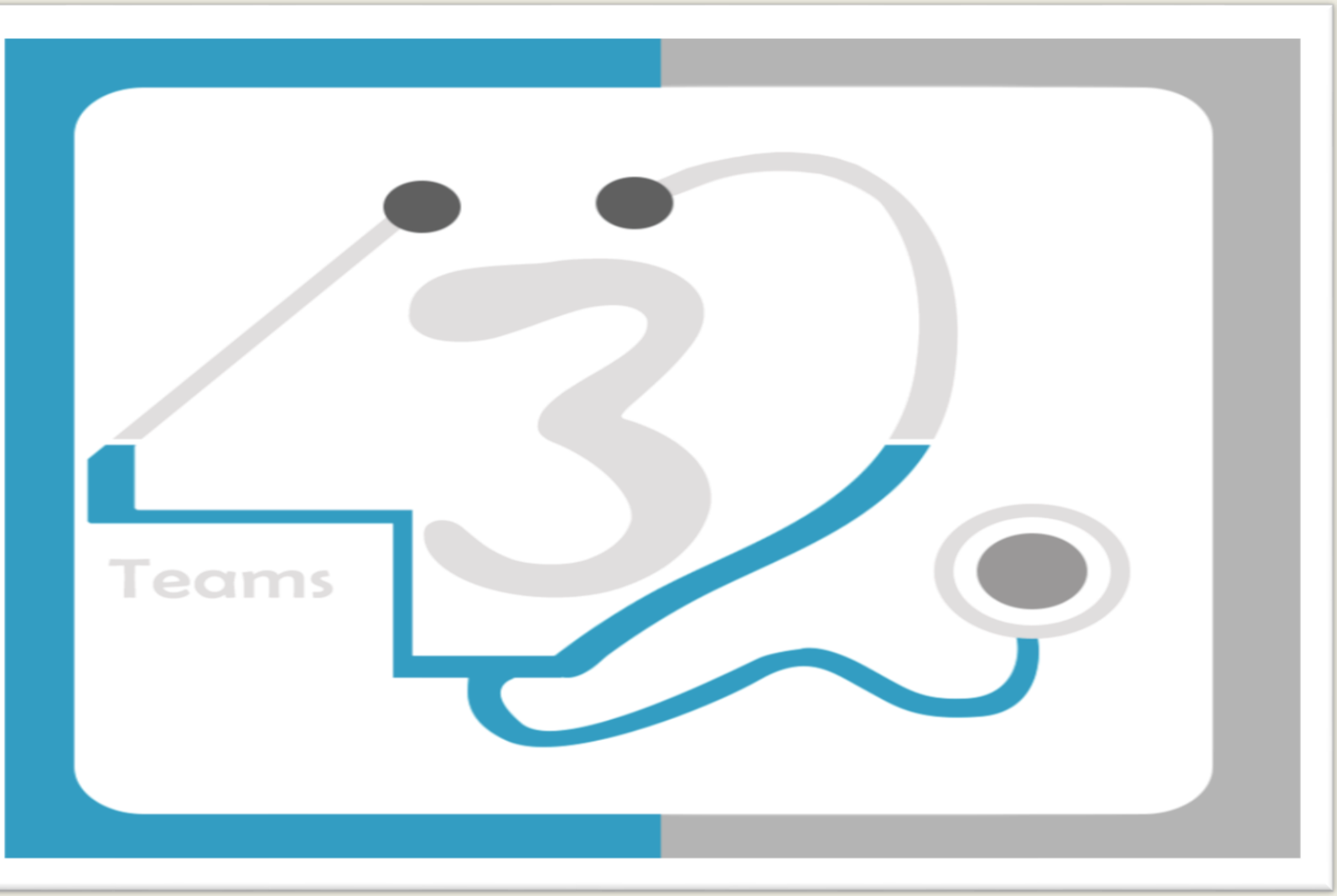

PHARMACOLOGY TEAM

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Pharmacology of drugs used in bronchial asthma

Contents:

WHAT THE DRUG DO???	TYPE Of The DRUG			
Bronchodilators • Quick relief medications • Treat acute episodic attack of asthma	B_2-adrenergic agonists --- Salbutamol terbutaline Salmetrol formetrol	Methylxanthines --- Theophyline Aminophyline	Muscarinic-receptor Antagonists --- Ipratropium Tiotropium	
Anti-inflammatory drugs • Control medications or prophylactic therapy. • Reduce the frequency of attacks.	Mast cell stabilizers --- Sodium cromoglycate Nedocromil	Corticosteroids --- Beclomethasone Fluticasone	Leukotrienes antagonists --- Zileuton (Lipooxygenase Inhibitors) Zafirlukast (Leukotrience Antagonists)	Anti-IgE monoclonal antibody --- Omalizumab
Drugs For cough				
Antibiotics				

First/ Bronchodilators

1. (B2-adrenergic agonists)

Sympathomimetics

β- Adrenoceptor agonists

Mechanism of action:

1. They stimulate beta-2 receptors directly, and they will stimulate adenyl cyclase. This stimulation will result in increase cAMP and then bronchodilation will happen.

2. Inhibit mediators release from mast cells.

3. Increase mucus clearance by increasing ciliary activity.

They divided into:

Non-selective β agonists

(Epinephrine – Isoprenaline)

Selective β2 – agonists

Short acting: (Salbutamol (albuterol)-Terbutaline)

Long acting: (Salmeterol-Formeterol)

NOTE :

1- We don't use Epinephrine for Bronchodilation because it's not selective

It works on all the receptors and it can sever vasoconstriction

Epinephrine is the Drug of choice for acute anaphylaxis

2- we don't use Norepinephrine for Bronchodilation because it doesn't work on B_2 receptors

E.g. : (Salbutamol, terbutaline, Salmetrol, formetrol) → **BY INHELATION**

IF orally → **tremors and Tachycardia**

Over doses cause

Tolerance

How can tolerance be overcome?

By using corticosteroid

When Long Acting like Salmetrol is preferred? In nocturnal asthma

If we give salbutamol as IV , it lead to hypokalemia

So, It's used for treatment of hyperkalemia

2. (Methyxanthins)

1- increasing the level of c-AMP via inhibtion of phosphodieasterase causing Bronchodilation

2- Theophyline is an universal antagonist at adenosine receptors causing smooth muscle relaxation

E.g. : (Theophyline), (Aminophyline) —Which is a mix of→ ***(Theophyline + ethylene))***

<u>Side Effects</u>: <u>Low therapeutic index</u>

GIT upset ; CNS stimulation ; CVS as tachycardi ; renal diuresis.

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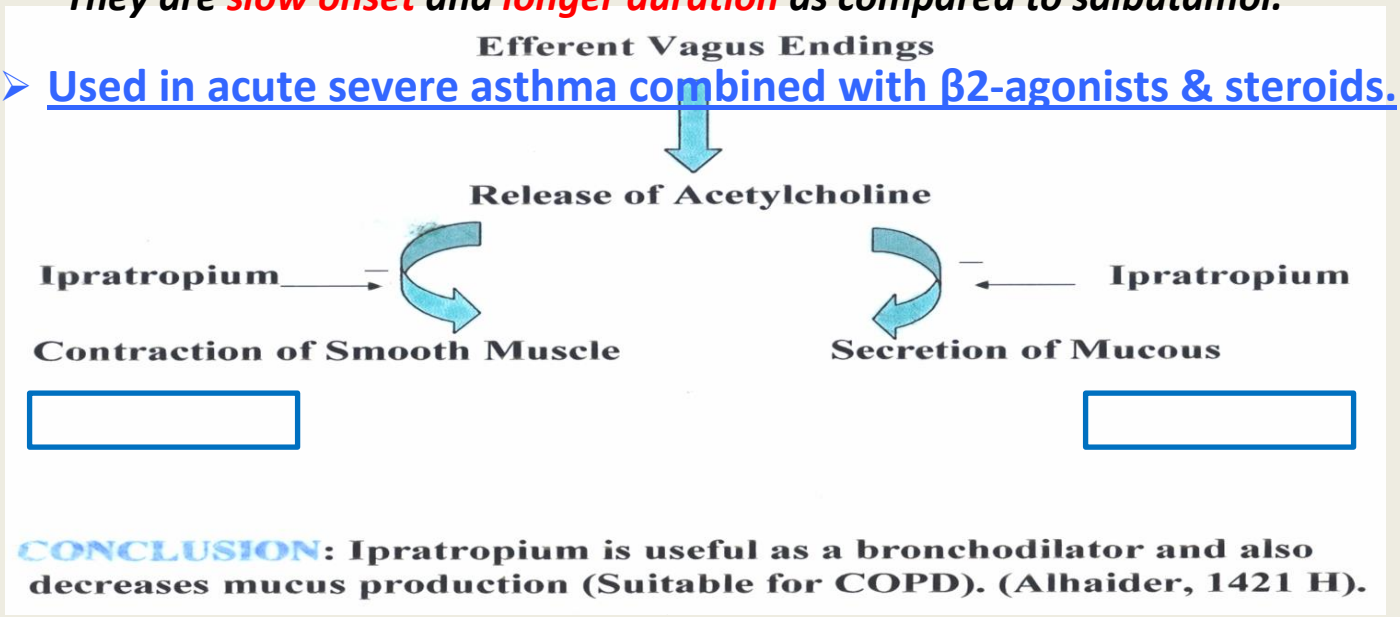
3. (Antimuscarinic Drugs)

They are slow onset and longer duration as compared to salbutamol.

- **<u>Used in acute severe asthma combined with β2-agonists & steroids.</u>**



Second \ Anti-inflammatory Drugs

These agents are not direct bronchodilators.

So, (Some of them are not effective to overcome the signs and symptoms)

1.(Mast cell stabilizers)

E.G. : (Sodium cromoglycate)

(Nedocromil)

These Drugs have better response in children

They block a calcium channel essential for mast cell degranulation, stabilizing the cell and

There by, preventing the release of histamine.

2.(Corticosteriods)

Mechanism of Action

Deacrese phospholipase A2

Inhibit the synthesis of arachidonic acid

Decrease leukocyte migration

Decrease inflammation

General examples : ***(Beclomethasone) ; (Fluticasone)***

PharmacoKinetics (How are they adminstrated???)

1- ***Oral**: (No salt and water retension)*

*example : **(prednisolone)***

tapering (decreasing the dose gradually) the dose of oral (prednisolone): Simply decrease the dose 5 mg every day. If the patient takes steroids for long time (more than 5 days).

Metabolic effects, **including:** **Hyperglycemia, decrease protein anabolism. Increase protein catabolism and stimulation of lipolysis – fat redistribution.**

2- ***Inhalation**: (mixed with long acting b2-agonist)*

Side Effects

- ***Cough***
- ***Dysphonia***
- ***Oral candidiasis***

*example : **(Beclomethasone)***

3- ***Injection** : (Injectable form of Corticosteriods are used for :*

Anaphylactic shock ---- status asthmaticus

*example: **(Hydrocortisone)***

Note that:

1. They have delayed onset of action (effect usually attained after 2-4 weeks).
2. They given as prophylactic medications, used alone or combined with beta-agonists.

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3. (Leukotriene-modifying agents)

Leukotrienes have multiple effects on the bronchi (inflammation, bronchoconstriction, increased vascular permeability...)

1- Lipooxygenase Inhibitors (Zileuton)

They cause other unwanted effects because they inhibit the whole pathway

2- (Zafirlukast) OR (Montelukast), it's more specific in action

Zafirlukast blocks the action of the cysteinyl leukotrienes on the CysLT1 receptors

Thus reducing constriction of the airways, build-up of mucus in the lungs and inflammation of the breathing passages.

***Side Effects ***

- increase PT if given with warfarin.

- Churg Strauss syndrome

- Elevation of liver Enzymes

- Indications

It's the drug of choice for aspirin sensitive (induced) asthma

4. (Anti-immunoglobulin E)

e.g. : (Omalizumab)

Mechanism of Action

Selective anti-IgE antibody that binds to IgE and prevents its association with IgE receptors, thus preventing allergen from activating mast cells

***Uses ***

For resistance type of asthma and allergic rhinitis

***Side effects ***

Infusion side effects

Mucolytics

They are drugs that maybe used in chronic pulmonary

E.G: (Acetylcysteine)

General note:

1. *drug of choice for COPD is Ipratropium.*
2. *Drug of choice for is b2-adrenergic agonist (short acting).*
3. *Drug of choice for severe form of COPD is Corticosteriods (oral or inhaler).*
4. *Drugs of choice for aspirin induced asthma are Leukotriene antagonist.*
5. *The patient given anti-inflammatory drugs to reduce the frequently of asthma.*
6. *Mast cell stabilization effect prevents the release of mediators.*
7. *First line treatment of asthmatic attack: selective $\beta 2$ agonists.*
8. *Long acting selective $\beta 2$ agonists have slow onset of action, so they are not used to relieve the acute episodes of asthma. They can consider as prophylactic.*
9. *In order to increase cAMP, we have to increase the synthesis of adenylyl cyclase and inhibit the degradation of cAMP.*

MCQs :

- ***Which drug of the following can not be used an asthma ?***

1- Salbutamol

2- Theophyline

3- terbutaline

4- Norepinephrine

- ***A petient comes to the clinic with severe asthma , he tried to take salbutamol but it didin't reveal the symptoms , what is the second treatment option you should adminstrate :***
  - ***1- Epinephrine***
  - ***2- Corticosteroid***
  - ***3- Mucolytics***
  - ***4- Leukotriene-modifying agents***

- ***A petient With asthma comes to you with GIT upset, renal diuresis after taking his medication what is the most possible drug that is causing his complains ?***
  - ***1- Omalizumab***
  - ***2- Zafirlukast***
  - ***3- Theophyline***
  - ***4- Beclomethasone***
- ***Oral candidiasis is a unique side effect for :***
  - ***1- Beclomethasone***
  - ***2- prednisolone***
  - ***3- Hydrocortisone***
  - ***4- Zafirlukast***

- ***The drug that binds to IgE preventing allergen from activating mast cells is :***
    1. ***Omalizumab***
    2. ***Zileuton***
    3. ***Salbutamol***
    4. ***Aminophyline***

Answer key \ (Q1 --- 4) (Q2 --- 2) (Q3 --- 3) (Q4 --- 1) (Q5 --- 1)