Pharmacology Team

Treatment of Asthma 2

Notes in light Blue

429 Medicine

Maha Al-Balharith Nasser Al-Wehaibi

badra'a Mouharib
Norhan Al-shamma'
Sarah Bin-Hussain
Arwa Al-Madani
Mohammed Alwatban

Designed by

Wejdan Al-Suwayyid Maha Al-Balharith

2. Anti-inflammatory Drugs:

by reducing inflammation in airways, they reduce the spasm of the airways & bronchial hyper-reactivity

Notes:
These agents are not direct bronchodilators.
Some of them are not effective to overcome the signs and symptoms of existing attack of asthma (But should be used).
Mainly used as prophylactic agents; thus therapeutic effects need weeks.

Anti-inflammatory Drugs

a. Mast cell stabilizers

e.g.: Sodium cromoglycate , Nedocromil.

PK: Available as inhaled aerosol or nebulizer solution.

Uses
- Prophylaxis in asthma especially in children.
- Allergic rhinitis.
- Conjunctivitis

Side Effects: Bitter taste, minor upper respiratory tract irritation (burning sensation, nasal congestion)

Disadvantage: Less effective in many asthmatics but better response in children.

b. Corticosteriods:

e.g. Beclomethasone; Fluticasone

MOA: Inhibit the synthesis of arachidonic acid; thus decrease leukocyte migration, phagolytic activity and inflammation) Also, they upregulate b-adrenoceptors.

PK:
Inhalation (metered-dose inhaler): Beclomethasone, fluticasone (high first pass effect in liver & low bioavailability) some of the drug during inhalation go to GIT so it should have side effects but it has high first pass metabolism so it is safe
orally: prednisone
Injection: (in sever cases) Hydrocortisone
(all these drugs ends with –sone)

Pharmacodynamics
- not bronchodilators it is only anti inflammatory
- reduce bronchial inflammation
- reduce bronchial hyper-reactivity to stimuli
- Effective in allergic, exercise, antigen and irritant-induced asthma.

- effect usually attained after 2-4 weeks (delayed onset of action).
- maximum action at 9-12 months. (in children can cause complete recover)
- given as prophylactic medications (to reduce frequency of asthma attacks)
- Abrupt stop of glucocorticoids should be avoided and dose should be tapered (adrenal insufficiency syndrome).

Glucocorticoids normally secreted by cortex of adernal gland If we take the drug that inhibit its secretion from our body so when we stop using the drug , it should be gradually until our body secrete it.

Uses

Inhalation

- relatively safe
- used as first-line treatment to control moderate to severe (if it is mild the bronchodilator be enough) asthma in children and adults alone or in combination with beta-agonists

oral/parenteral corticosteroids produce systemic effects (toxicity) & are reserved for:

- management of acutely ill patients
- Status asthmaticus (i.v.).

..:: ALL treatment of Status asthmaticus is IV ::..

Side effects of Inhaled corticosteroids:

Cough
difficult or painful speech (Dysphonia)
Possible growth retardation in children.
Oral candidiasis

— **NOTE:**
— -Corticosteroids combine with:
— -B2 agonist
— -Antimuscarinics
— -antileukotriene
—

Note:
Adrenal gland suppression: the gland secrets corticosteroids.
But when you take corticosteroids drug every day the gland won't secret because the body has already have it from the drug >> this is when you take it at night .
The gland secret in 6 mornings.
* This can be avoided by giving the drug at 7 :00 a.m. Because it will give the adrenal gland the time to secret corticosteroids before taking the drug

c. Leukotriene-modifying agents

1) Leukotrience synthesis inhibitors (Lipooxygenase Inhibitors) e.g. Zileuton
2) Leukotrience Antagonists e.g Zafirlukast ,Montelukast
PK: These drugs are available as oral form but with side effects less than corticosteroids

- **5-Lipoxygenase inhibitors**

Zieluton

is a selective inhibitor of 5-lipo-oxygenase
inhibits synthesis of leukotrienes (LTB4 , LTC4, LTD4& LTE4).
Given orally
Short duration of action.
Is given (3-4 times/ day).

- **Leukotriene receptor antagonists**

Zafirlukast

are selective, reversible inhibitors of cysteinyl leukotriene receptors (LTD4)
Taken orally.

Uses of antileukotriene drugs
(Zafirlukast & Zieluton)
Used for prophylaxis of mild to moderate asthma
Aspirin-induced asthma
Prevention of antigen and exercise-induced asthma
Are not effective to relieve acute attack of asthma

NOTE:
-Aspirin-induced asthma: Aspirin inhibit COX, so all arachidonic acid shift to lipoxygenase pathway so more leukotriene.
-To treat this type we use anti leukotriene.

Side Effects:

-increase PT if given with warfarin.
- Churg Strauss syndrome

NOTE:
Why they are not inhalers??
Because we want to inhibit all lukotrines in the body

Indications:
Preventive medication in those who have difficulty with inhalers or side effects from inhaled corticosteroids.
Management of aspirin sensitive asthma.

NOTE:
Patients with aspirin-induced asthma, may show strong or week response to Leukotriens antagonists?
Strong

Anti-immunoglobulin E (e.g. Omalizumab)

(any drug ends with –mab is monoclonal antibody so it is protein can't given orally but SC)

When a drug ends with mab :

-new
-IV
-expensive

MOA:
Selective anti-IgE monoclonal antibody that binds to IgE and prevents its association with IgE receptors, thus preventing allergen from activating mast cells or basophiles
Decreases serum IgE
Due to the above effects, omalizumab decreases the numbers of eosinophils, T and B lymphocytes
Uses: for resistance type of asthma and allergic rhinitis.

Side effects and Limitations:
Infusion side effects and expensive.

Treatment of COPD

-Chronic irreversible airflow obstruction
-Smoking is a high risk factor
-Inhaled bronchodilators
-Inhaled antimuscarinics **(main drug)**
-Short acting bronchodilators
-these drugs can be used either alone or combined

Examples
-Salbutamol (short acting B2 agonist) + ipratropium (anti muscarinic)
-Salmeterol (long actinig B2 agonist) + Tiotropium (anti muscarinic its duration 24 h). (long acting-less dose frequency)

For severe COPD
-Bronchodilators
-Inhaled glucocorticoids
-Oxygen therapy
- Antibiotics

NOTE:
COPD : pathologic damage Anti-inflammatory is used with COPD when there is infection
Asthma: inflammation always occur

Does treatment of COPD differs from bronchial Asthma?

- More specific ,the antibody go to the IgE→ prevent allergen binding → mast cell and basophile inactivation

COPD →CO_2 retention
Asthma → no CO_2 retention .

NOTE in non-selective B agonist :
Adrenaline → β_1 , α_1 , β_2
Nor-adrenaline→β_1 , α , NOT β_2

Summary for treatment of asthma

Anti-inflammatory drugs (prophylactic)

Corticosteroids Dexamethasone, Fluticasone	Inhibits phospholipase A2 inhalation
prednisolone	Orally
Hydrocortisone	parenterally
Mast stabilizers Cromoglycate	Inhalation Prophylaxis in children
Cysteinyl antagonists Zileuton (5 lipooxygenase inhibitor) Zafirlukast (D4 blocker)	(orally) (orally)
Omalizumab	Injection SC Anti IgE antibody

Questions to remind u some points in lecture

the most potent anti inflammatory drug is ?

Corticosteroids cause it inhibits phospholipase A2 so inhibit all the pathway of inflammation

Mast stabilizers has better response in?

Children

Aspirin-induced asthma can be treated with?

antileukotriene drugs: Zileuton (5 lipooxygenase inhibitor) and Zafirlukast (D4 blocker) which are taking orally and have anti inflammatory + bronchodilator effect.

Omalizumab should be taking by?

SC because it is monoclonal antibody (anti IgE)

One Example of the combonation which use in COPD?

Salbutamol + ipratropium

Done by : Badra'a

Study Questions

Choose the ONE best answer.

27.1 A 12-year-old girl with a childhood history of asthma complained of cough, dyspnea, and wheezing after visiting a riding stable. Her symptoms became so severe that her parents brought her to the emergency room. Physical examination revealed diaphoresis, dyspnea, tachycardia, and tachypnea. Her respiratory rate was 42 breaths per minute, pulse rate 110 beats per minute, and blood pressure 132/65 mm Hg. Which of the following is the most appropriate drug to rapidly reverse her bronchoconstriction?

A. Inhaled cromolyn.

B. Inhaled beclomethasone.

C. Inhaled albuterol.

D. Intravenous propranolol.

27.2 A 9-year-old girl has severe asthma, which required three hospitalizations in the last year. She is now receiving therapy that has greatly reduced the frequency of these severe attacks. Which of the following therapies is most likely responsible for this benefit?

A. Albuterol by aerosol.

B. Cromolyn by inhaler.

C. Fluticasone by aerosol.

D. Theophylline orally.

E. Zafirlukast orally.

View Answer

27.3 A 68-year-old male retired police officer who has smoked a 1/2 pack of cigarettes a day for the past 40 years is diagnosed with chronic obstructive pulmonary disease (COPD). He has a difficulty in expiration during breathing, but the symptms are mild and intermittent. Which one of the following agents would most appropratate initial therapy.

A. Systemic corticosteroids

B. Albuterol

C. Salmeterol

D. Tiotropium plus salmeterol

E. Theophylline

View Answer