



RESPIRATORY SYSTEM НАЧАТ ВАТСН

SUBJECT : Pharmacology LEC NO. : DONE BY : Anas zakarneh

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Respiratory system (Pharmacology)

- Lecture 1: Treatment of COPD
- Lecture 2: Treatment of Asthma 1
- Lecture 3: Treatment of Asthma 2
- Lecture 4: Treatment of allergic rhinitis + cough
- Lecture 5: Treatment of bacterial respiratory infections 1
- Lecture 6: Treatment of bacterial respiratory infections 2
- Lecture 7: Treatment of tuberculosis (TB)





Lecture 1: Treatment of Chronic Obstructive Pulmonary Disease (COPD)

Respiratory system Second year Medical school Hashemite University 2nd semester 23/24 Sofian Al Shboul, MD, PhD.



Lecture objectives

- Review the pathophysiology of COPD
- Understand COPD therapeutic approach
- Describe the mechanisms of action (MOA), pharmacokinetics and side effects of agents used for COPD management





Facts & numbers

- Nearly half COPD patients say it limit their work and social activity
- Known as disease of old age but can occur as young as 35 years

CHRONIC OBSTRUCTIVE PULMONARY DISEASE



curable but trea

- <u>SMOKING</u>
- Approximately 15-20% of the cases occur in nonsmokers.



Definition & sub-types





airways"

CHRONIC





Pathogenesis

- Chronic bronchitis and emphysema: CD8+ T-lymphocytes, neutrophils, and CD68+ monocytes/macrophages in the airways.
- the bronchial inflammation of asthma: presence of CD4+ Tlymphocytes, eosinophils, and increased interleukin (IL)-4 and IL-5.







- Dyspnea
- Chronic cough
- Sputum production
- Wheezing and chest tightness
- Breathlessness
- Difficulty sleeping
- Fatigue.







Treatment & management

quit smoking بده يكون pharmacological cause المسبب الرئيسي بس مش pharmacological cause بده يكون دواء أما إذا طلب pharmacological cause

- Quit smoking
- education and counselling (about COPD an inhaler techniques).
- Seasonal influenza and COVID-19 vaccinations.
- Diet: no ideal COPD diet but excess weigh can contribute to dyspnea >>> normal bod mass index (BMI).







The main

- COPD pharmacological treatment include
- 1. Short-acting β_2 agonists (SABAs)
- 2. Long-acting β_2 agonists (LABAs)
- 3. Short-acting muscarinic antagonist (SAMA)
- 4. Long-acting muscarinic antagonist (LAMA)
- 5. Inhaled corticosteroids (ICS)
- 6. Combinations of these classes
- 7. Vaccines, antibiotics and other agents

The mainstays of drug therapy for stable symptomatic COPD are inhaled bronchodilators (beta-agonists and muscarinic antagonists).





Pharmacological agents

MEDICATION	INI	LONG-ACTING β_{2} ADRENERGIC AGONIST/CORTICOSTEROID COMBINATION	
SHORT-ACTING β_2 ADRENERGIC AGONISTS (SABAs)		Formoterol/budesonide SYMBICORT	Asthma, COPD
Albuterol PROAIR, PROVENTIL, VENTOLIN	Asthma, COPD	Salmeterol/fluticasone ADVAIR	Asthma, COPD
Levalbuterol XOPENEX	Asthma, COPD		houma, corb
LONG-ACTING β_2 ADRENERGIC AGONISTS (LABAs)		SHORT-ACTING ANTICHOLINERGIC	
		Ipratropium ATROVENT	Allergic rhinitis, Asthma, COPD
Formoterol FORADIL, PERFOROMIST	Asthma, COPD	SHORT-ACTING β 2 AGONIST/SHORT-ACTING ANTICHOLINERGIC COMBINAT	ON
			COPD
Olodaterol Striverdi Respimat	COPD	LONG-ACTING ANTICHOLINERGIC (LAMA)	
Salmeterol SEREVENT	Asthma, COPD		
INHALED CORTICOSTEROIDS		Glycopyrrolate SEEBRI NEOHALER	COPD
		/ Fiotropium SPIRIVA	Asthma, COPD
Budesonide PULIMICORT, RHINOCORT*	Allergic rhinitis, Asthma, COPD		
	,	LABA/LAMA COMBINATION	
Fluticasone ELONASE*, ELOVENT	Allergic rhinitis, Asthma, COPD		COPD
Mometasone ASMANEX, NASONEX*	Allergic rhinitis, Asthma		
			COPD

OTHER AGENTS	
Roflumilast DALIRESP	COPD
Theophylline ELIXOPHYLLIN, THEO-24	Asthma, COPD

copd +asthamaكلهم لل إلا اللي عليهم نجمه للcopd بس





				-				
SABAs (Short- Acting Beta Agonists)	LABAs (Long- Acting Beta Agonists)	ICS (Inhaled Corticoste roids)	LABAs+ICS	SAMA (Short- Acting Muscarinic Antagonist)	SABA/SAM A	LAMA (Long- Acting Muscarinic Antagonists)	LABA/LAMA	others
Albuterol	Salmeterol	Fluticason e	Salmeterol/ Fluticasone	Ipratropium	Albuterol/Ip ratropium	Glycopyrrol ate	Formoterol/ Glycopyrrol ate	Roflumilast
Levalbuterol	Formoterol	Budesonid e	Formoterol/ Budesonide			Tiotropium	Olodaterol/ Tiotropium	Theophyllin e
	Olodaterol	Mometaso ne	Formoterol/ Mometason e					





Just ignore it

مش حيجي منه

Pharmacological agents

Subclass	Mechanism of Action	Effects	Clinical Applications	Pharmacokinetics, Toxicities	
BETA AGONISTS					
Albuterol	Selective β_2 agonist	Prompt, efficacious bronchodilation	Asthma, chronic obstructive pulmonary disease (COPD) • drug of choice in acute asthmatic bronchospasm	Aerosol inhalation • duration several hours • also available for nebulizer and parenteral use • Toxicity: Tremor, tachycardia • overdose: arrhythmias	
Salmeterol	neterol Selective β ₂ agonist Slow onset, primarily preventive action; potenti- ates corticosteroid effects		Asthma prophylaxis	Aerosol inhalation • duration 12–24 h • <i>Toxicity</i> : Tremor, tachycardia • overdose: arrhythmias	
 Metaproterenol, terbutaline: Simi Formoterol: Similar to salmeterol 	lar to albuterol; terbutalin	e available as an oral drug			
CORTICOSTEROIDS, INHALED					
Fluticasone	Alters gene expression Reduces mediators of inflammation • powerful prophylaxis of exacerbations		Asthma • adjunct in COPD • hay fever (nasal)	Aerosol • duration hours • Toxicity: Limited by aerosol application • candidal infection, vocal cord changes	
Beclomethasone, budesonide, flunisolide, others: Similar to fluticasone					
CORTICOSTEROIDS, SYSTEMIC					
Prednisone	Like fluticasone	Like fluticasone	Asthma • adjunct in COPD	Oral • duration 12–24 hours • <i>Toxicity</i> : Multiple • see Chapter 39	
Methylprednisolone: Parenteral agent like prednisone					
METHYLXANTHINES					
Theophylline	Uncertain • phosphodiesterase inhibition • adenos- ine receptor antagonist	Bronchodilation, cardiac stimulation, increased skeletal muscle strength (diaphragm)	Asthma, COPD	Oral • duration 8–12 h but extended-release preparations often used • <i>Toxicity</i> : Multiple (see text)	



Pharmacological agents:



β2-adrenergic agonists (adrenergic β2 receptor They will go to the beta 2 receptor and then will bind with the receptor agonists): شوبعمل الreceptor أصلا؟

act on the $\beta 2$ adrenergic receptor:

 \rightarrow smooth muscle relaxation drugs ماي المم اشي و الثلاثة الباقيين الهم علاقة بال dilation of bronchial passages

➢ vasodilation in muscle and liver ➢ relaxation of uterine muscle

 \succ release of insulin.

and they will do what the receptor can do

Beta 2 receptor :vasodilation/ bronchodilation / release glucose /release of insulin /relaxtion So it's act on relaxation/dilation part



Primarily used to treat asthma and COPD.



Pharmacological agents: β2-adrenergic agonists

VIP

► MOA: You need to know the steps

Receptor activation (G protein (Gs) + adenylyl cyclase) >> increases intracellular cAMP >> activate protein kinase A (PKA) >> reduce intracellular Ca2+ or decrease the sensitivity of Ca2+ >> inhibition of myosin light chain phosphorylation (MLCK) >> preventing airway smooth muscle contraction.

برضومهم → Anti-inflammatory effects? reducing intercellular adhesion molecule-1 (ICAM-1) reducing granulocyte-macrophage colonystimulating factors (GM-CSF) release





Pharmacological agents: β2-adrenergic agonists

 β 2-adrenergic agonists (adrenergic β_2 receptor agonists):

✤Side effects:

See the figure

All β2 agonists are available in inhaler form: metered-dose inhalers (MDI) or dry powder inhalers (DPI)

مش مطلوب للامتحان:Answer







Pharmacological agents: muscarinic antagonist

COPD pharmacological treatment include

- 3. Short-acting muscarinic antagonist (SAMA)
- 4. Long-acting muscarinic antagonist (LAMA)

✓ Side effects: dry mouth, constipation and urinary retention

These drugs will block the (M3) to prevent airway smooth muscle contraction

muscarinic antagonist (muscarinic receptor antagonist

شو بساوي ؟

ىشتغلو عكس الmuscarinic

(MRA): All drugs here will try to dayloid the bronchi

- ✓ Muscarinic receptors are predominately present on glandular cells, smooth muscle cells, and cardiac muscle cells.
- Competitively inhibit the effect of acetylcholine (ACh) at muscarinic receptors (M1 and M3)
- ✓M1: CNS

✓ M3: smooth muscle GI, UT, airway, and blood vessels
 GI/UT/airways مهم نعرف انو الm3 موجود بال



Mechanism of action of muscarinic antagonists







Pharmacological agents: Inhaled corticosteroids (ICS)

COPD pharmacological treatment include

5. Inhaled corticosteroids (ICS)



<mark>inhibit the release of arachidonic acid through inhibition of phospholipase A2</mark> راح نتعمق فيهم بسنة ثالثة

هسا بدنا ناخذ التفاصيل اللي بتهمنا

Oral glucocorticoids can be effective in treating an acute exacerbation **BUT** generally they are not recommended



 Anti-inflammatory agents that should be reserved for patients with frequent or severe exacerbations and high blood eosinophils (~10%) of the COPD population), or those with concomitant asthma

Inhaled corticosteroids (ICS)

They are used in all diseases and symptoms وين ما تحطهم يشتغلو بس هون راح نركز على اللي بكونو بخاخات مش الoral

- Do not relax airway smooth muscle directly but reduce bronchial reactivity and potentiate the effects of β -receptor agonists
- Main effect: inhibition of the infiltration of lymphocytes, eosinophils, and mast cells.

بالعادة ما ينعطي لحالو بكون معو دواء ثاني و إذا كان لحاله بكون عشان inflammatory process تاعته

Pharmacological agents: **Drug combinations**

COPD pharmacological treatment include

6. Combinations of different drug classes

LABA+ corticosteroids

	LONG-ACTING β_{2} ADRENERGIC AGONIST/CORTICOSTEROID COMBINATION						
	Formoterol/budesonide SYMBICORT	Asthma, COPD					
	Formoterol/mometasone DULERA	Asthma, COPD					
	Salmeterol/fluticasone ADVAIR	Asthma, COPD					
SABA+	SHORT-ACTING B2 AGONIST/SHORT-ACTING ANTICHOLINERGIC COMBINAT	ION					
SAMA for	Albuterol/ipratropium COMBIVENT RESPIMAT, DUONEB	COPD					
COPD	LONG-ACTING ANTICHOLINERGIC (LAMA)						
only							
-							
	Formoterol/glycopyrrolate BEVESPI AEROSPHERE	COPD					
	Olodaterol/tiotropium STIOLTO RESPIMAT	COPD					

LABA+ LAMA for COPD





SABAs (Short- Acting Beta Agonists)	LABAs (Long- Acting Beta Agonists)	ICS (Inhaled Corticoste roids)	LABAs+ICS	SAMA (Short- Acting Muscarinic Antagonist)	SABA/SAM A	LAMA (Long- Acting Muscarinic Antagonists)	LABA/LAMA	others
Albuterol	Salmeterol	Fluticason e	Salmeterol/ Fluticasone	lpratropium	Albuterol/Ip ratropium	Glycopyrrol ate	Formoterol/ Glycopyrrol ate	Roflumilast
Levalbuterol	Formoterol	Budesonid e	Formoterol/ Budesonide			Tiotropium	Olodaterol/ Tiotropium	Theophyllin e
	Olodaterol	Mometaso ne	Formoterol/ Mometason e					

إذا حفظت الحدول يتحل كل اسبئلة الدكتون



Pharmacological agents:

Other agents

الوحيد اللي بدنا نعرفه من الothers others

* Oral phosphodiesterase-4 (PDE4) inhibitor

* Reduces exacerbations in patients with severe chronic bronchitis. Not emphysema

* <u>Reduce inflammation</u> by increasing levels of intracellular cAMP in lung cells.

PDE4: (inhibit bronco dilation) اهو إنزيم بوقف كل اشي بالرسمة فأنا بس اعمله inhibiting بزيد فعالية كل اشي هيك بده الدكتور





Pharmacological agents:

Other agents

• <u>Roflumilast</u>

- NOT a bronchodilator and is NOT indicated for the relief of acute bronchospasm, it decreases inflammation in lungs
- Used in treating those with chronic bronchitis and a history of exacerbations.
- Use is limited by common adverse effects including weight loss, nausea, diarrhea, and headache. used with caution in those suffering from depression. Or mental issue

VIP



Pharmacological agents: Other agents

موجود بالشا*ي*

- Methylxanthines such as theophylline which has mild bronchodilatory effect in stable COPD. Theophylline is seen to improve breathlessness when used as an add-on to salmeterol. Methylxanthines are not recommended for use in exacerbations due to adverse effects.
- Cough medicines are not recommended, Beta blockers are not contraindicated for those with COPD and should only be used where there is concomitant cardiovascular disease

احتمال كبير تيجي هاي الفقره بالامتحان



Sofian Al Shboul ©

CAT & mMRC scales

Range of CAT scores from 0–40. Higher scores denote a more severe impact of COPD on a patient's life.

How is your COPD? Take the COPD Assessment Test[™] (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.





مش مطالبين بالسلايد للامتحان بس حلو تقراهم

Modified Medical Research Council (mMRC) dyspnea scale

Grade	Description of breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing





Treatment plans

هون مريض معه COPD

اللي بهمني انو أقيم كم مره صار عنده moderate exacerbations او كم مره دخل المستشفى





GOLD ABE assessment tool.







Sofian Al Shboul ©





Initial pharmacological treatment



الأصفر قراية

If there is an indication for an ICS, then LABA+LAMA+ICS has been shown to be superior to LABA+ICS and is therefore the preferred choice

The use of LABA+ICS in COPD is no longer encouraged.

#: single inhaler therapy may be more convenient and effective than multiple inhalers Exacerbations refers to the number of exacerbations per year

Sofian Al Shboul ©



Follow-up pharmacological treatment.



Alvar Agustí et al. Eur Respir J 2023;61:2300239

Quiz time

1- A 58-year-old woman with COPD has been hospitalized three times in the past year for COPD exacerbations. She reports only mild symptoms between exacerbations. Her regimen for the past year has included inhaled salmeterol twice daily and inhaled tiotropium once daily. Her current FEV1 is below 60%. Which is an appropriate change in her drug therapy?

A. Discontinue the tiotropium.

B. Discontinue the salmeterol.

c. Change the salmeterol to a combination product that

includes both a LABA and an inhaled corticosteroid(for example, salmeteroVfluticasone DPI).

D. Add theophylline.

2- A 58-year-old man who is a smoker with chronic obstructive pulmonary disease (COPD) presents to the emergency department (ED) with shortness of breath and a productive cough. This is the fourth time this year he has come to the ED because of COPD exacerbation. After this hospital stay, his primary care physician prescribes roflumilast in hopes of decreasing his ED visits for COPD exacerbation. What is roflumilast's mechanism of action?

Ans 1)C 2)D 3)A 4)C

(A) Blocks arachidonic acid production

(B) Bronchodilation

(C) Inhibition of leukocyte chemotaxis by interfering with microtubules

(D) PDE4 inhibitor

(E) Thins and loosens mucus

3-What is the first line treatment option for COPD?

- A- Bronchodilator
- B- Muscarinic agent
- C- Corticosteroids
- D- None of the above

4-Roflumilast is a medication that belongs to class of:

- A- Anticholinergics
- B- Methylxanthines
- C- Phosphodiesterase inhibitors
- D- Long-acting beta agonist