

L2.

Beta adrenergic blockers

EDITING FILE

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مشاكل قلبك الواجد بتخضع
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Objectives:

- Outline the mechanisms of action of β -blockers
- Classify β -receptor blockers into selective & non-selective
- Know the pharmacokinetic aspects & pharmacodynamic effects of β -adrenergic blockers.
- Identify the specific uses of non-selective and selective β -adrenergic blockers.



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β -Adrenoceptors Blockers

- Beta-blockers are a group of drugs that inhibit the sympathetic activation of β -adrenergic receptors.
- All drugs end in **-olol**

Pharmacodynamic
classification

According to selectivity

Non-selective β -Antagonists blocks β_1 & β_2 receptors

(STOP):

"O \rightarrow Z"

Sotalol, Timolol(Eye)
Oxprenolol **Propranolol**,
Pindolol

Selective β_1 antagonists

(Cardiogenic) "A \rightarrow M"

"ABCEM":

Acebutolol, Atenolol,
Bisoprolol, Betaxolol,
Celiprolol, Esmolol,
Metoprolol

Mixed α , β receptors blockers:

Carvedilol,
Labetalol

β -Adrenoceptors Blockers

Pharmacodynamic classification (Conti.)

According to **presence of agonistic/antagonistic action** According to presence of According to selectivity
“Intrinsic Sympathomimetic membrane stabilizing effects Activity”(ISA)

Without ISA β -antagonists blocks Drugs:

(Pure antagonists, 100% blocks receptor) Atenolol, Bisoprolol ,Sotalol ,Timolol, Metoprolol, Propranolol, Carvedilol

With ISA (may activate beta receptor, with a partial agonist effect):
Acebutolol, **Pindolol**, **Oxprenolol** , Celiprolol.

Drugs:
Propranolol, labetalol.

According to **presence of membrane stabilizing effects**

Effect:

- **Block Na Channels** (makes muscle cells unresponsive to pacemaker stimulation \rightarrow \downarrow excitability \rightarrow no action potential \rightarrow \downarrow contraction of muscles) so it works as local anesthetic.
- **Quinidine-like action** (Quinidine is a class of antiarrhythmic drugs).
- **Antiarrhythmic action.**



Pharmacokinetic Classification

According to lipid solubility

Drug	Oral absorption	Liver metabolism & excreted in urine	T1/2	CNS side effects i.e. Drugs Sedative effect ↓ Anxiety effects	Drugs
lipophilic / hydrophobic	complete "given orally"	Yes "Undergo hepatic clearance"	short "Because it'll reach the liver faster"	High	Metoprolol, Labetalol, Propranolol , Carvedilol, Timolol,
Hydrophilic	Irregular "giving IV"	No "Undergo renal clearance"	long	Low	Bisoprolol, Esmolol, Atenolol, Sotalol.

Most of them are lipid soluble

- Well absorbed orally.
- Rapidly distributed, cross readily BBB
- Most of them have half-life from 3-10 hrs except **Esmolol** (10 min. given intravenously).
- Most of them are metabolized in liver & excreted in urine.





Effect of β agonists



Rc	tissue	action
β_1	Heart: <ul style="list-style-type: none">• Sinus & AV• Conduction pathway• Myocardial fibrils• Kidney ('JG' cells) 'JG' = juxtaglomerular cells "found in the kidneys for the stimulation of renin release"	<ul style="list-style-type: none">• +ve Chronotropic (\uparrow heart Rate) causes tachycardia• +ve Inotropic (\uparrow contractility)• +ve Dromotropic (\uparrow conduction velocity) "يزيد انتقال الإشارات from the pacemaker to ventricles therefore the force of contraction increases" <ul style="list-style-type: none">• renin release• \uparrow Automaticity
β_2	<ul style="list-style-type: none">• vascular & bronchial smooth muscles• Liver• Skeletal muscles	<ul style="list-style-type: none">• Relaxes smooth muscles• Bronchial & Vascular dilation while α_1 receptor causes vasoconstriction• Hyperglycemia due to:<ul style="list-style-type: none">\uparrow Glycogenolysis (breakdown of glycogen into glucose) & gluconeogenesis (formation of new glucose) in liver\uparrow Release of glucagon from pancreas\uparrow Release of NE from (Pre-synaptic β_2 receptors). "Positive feedback mechanism on sympathetic system".
β_3	Adipose tissue	\uparrow Lipolysis by adipose tissue

Effects of β blockers

1

CVS:

Negative inotropic, chronotropic, dromotropic \rightarrow \downarrow CO

Antianginal effects (ischemic heart disease):

- \downarrow Heart rate (bradycardia)
- \downarrow force of contraction cardiac work.
- \downarrow Oxygen consumption due to bradycardia .

in angina the blood flow to the heart is reduced so we give the patient β blockers to reduce the force needed for normal cardiac output.

Anti-arrhythmic (irregularity in heart rate) effects:

- \downarrow excitability causes Bradycardia, - \downarrow automaticity & \downarrow conductivity (due to its sympathetic blocking).

in arrhythmia the automaticity highly increases so we use β blockers in this condition to decrease it.

Blood vessels β_2 :

- \uparrow peripheral resistance (PR) by blocking vasodilatory effect of β_2 causing vasoconstriction.
- \downarrow blood flow to organs (cold extremities)

“contraindicated in peripheral diseases like Reynaud's disease”

Antihypertensive: \downarrow BP in hypertensive patients due to effects on:

📌 β_1 Blockade:

- Inhibiting heart properties \rightarrow \downarrow cardiac output
- \downarrow renin secretion Ang II & aldosterone secretion Renin increases BP by 2 main mechanisms:
 - 1) Direct arteriolar vasoconstriction (Ang II is the strongest vasoconstrictor mediator in our body)
 - 2) \uparrow Aldosterone \rightarrow \uparrow Na & water retention \rightarrow \uparrow blood volume

📌 Pre-synaptic β_2 Receptors blockade:

- Presynaptic inhibition of NE release from adrenergic nerves opposite to the positive feedback of the agonists.

Effects of β blockers

2



Respiratory tract $\beta 2$

Bronchoconstriction

“**contraindicated in asthmatic patients.**”

Unless if selective $\beta 1$ blockers were given not $\beta 2$ Because it will only act on the heart without affecting the lungs.

3



Eye

- \downarrow Aqueous humor production from ciliary body
- \downarrow Reduce intraocular pressure (IOP)

✦ **e.g., timolol used in treatment of glaucoma as eye drops** ✦

4



Intestine & Metabolic effect

- \uparrow Intestinal motility
- Hypoglycemia due to:
 - \downarrow Glycogenolysis in liver,
 - \downarrow Glucagon secretion in pancreas &
 - \downarrow Lipolysis in adipocytes
- Na^+ retention: secondary to \downarrow BP \rightarrow \downarrow renal perfusion

Clinical uses of β receptor blockers

CVS disorders	hypertension	<ul style="list-style-type: none">• Propranolol, atenolol, bisoprolol• Labetalol: α, β blockers in hypertensive pregnant & hypertensive crisis.
	Arrhythmia	<ul style="list-style-type: none">• In supraventricular & ventricular arrhythmias.• Esomolol, Bisoprolol and carvedilol are preferred
	Angina pectoris	<ul style="list-style-type: none">• \downarrow heart rate, \downarrow cardiac work & oxygen demand.• \downarrow the frequency of angina episodes.• Atenolol, Bisoprolol, Metoprolol (β1 Selective)
	myocardial infraction	<ul style="list-style-type: none">• Have cardio-protective effect (\downarrow infarct size, \downarrow morbidity & mortality, \downarrow Myocardial myocardial O2 demand)• Anti-arrhythmic action.• \downarrow incidence of sudden death.
	Congestive heart failure	<ul style="list-style-type: none">• Bisoprolol, Metoprolol (selective β1-blockers)• carvedilol (non-selective α,B blocker) <p>Helps in:</p> <ul style="list-style-type: none">• Antioxidant• \downarrow myocardial remodeling• \downarrow risk of sudden death.
	pheochromocytoma	<ul style="list-style-type: none">• ✦ used with α-blockers (never alone) ✦• α-blockers lower the elevated blood pressure.• β-blockers protect the heart from NE.

CVS disorders (Conti.)

Chronic glaucoma

- **Timolol as eye drops:**
- ↓ aqueous humor production by ciliary body.
- ↓ Intraocular pressure (IOP)

Hyperthyroidism
(thyrotoxicosis)
caused by the over
secretion of the thyroid
hormone

- Protect the heart against sympathetic stimulation (thyrotoxicosis)
- Controls symptoms: Tachycardia, tremors & sweating

Migraine headache
(Prophylactic)

- reduce episodes of chronic migraine Migraine (Prophylactic)
- catecholamine-induced vasodilatation in the brain vasculature
- **e.g: Propranolol**

Anxiety
(Somatic symptoms)

- “The social and performance type”**
- **Propranolol:** controls symptoms due to sympathetic system stimulation as tachycardia, tremors, sweating .
 - it dose not control the psychological symptoms.
 - **It is commonly used due to its mild effects.**

ADRs of β -blockers

General	<ul style="list-style-type: none">• Depression, hallucinations, Fatigue• Gastrointestinal disturbances, Sodium retention		
β1 Block	Bradycardia	Hypotension	Heart block
β2 Block “only with non- selective β blockers”	<ul style="list-style-type: none">• Hypoglycemia.• \uparrow TG \rightarrow Hypertriglyceridemia.• Bronchoconstriction (Contraindicated in Asthma, emphysema).• Cold extremities & intermittent claudication (due to vasoconstriction).• Erectile dysfunction & impotence• Coronary spasm \rightarrow in variant angina patients		

- ♦ All β -Adrenergic blockers mask hypoglycemic manifestations in **diabetic** patients i.e. tachycardia, sweating \rightarrow COMA. ♦ the symptoms of hypoglycemia that are usually associated with the disease won't appear in case of using these drugs so we need to use it cautiously.
- **Sudden stoppage** will give rise to a **withdrawal syndrome**: Rebound angina, arrhythmia, myocardial infarction & Hypertension
 - **WHY ?**: Due to Up-regulation of β -receptors.
- To prevent withdrawal manifestations \rightarrow drug withdrawn **gradually**.

contraindication of β -blockers

1

Heart Block
(β -blockers can precipitate heart block).

2

Bronchial Asthma
(safer with cardio-selective β 1-blockers).

3

Peripheral vascular disease
(safer with cardio-selective β -blockers).

4

Diabetic patients
Masking of hypoglycemia
GIVEN CAUTIOUSLY.

5

Hypotension

6

Alone in pheochromocytoma
(must be given with an α -blockers)

Propranolol

Prototype

MOA		<ul style="list-style-type: none">• Non-Selective Competitive Blocker of β_1 & β_2• Membrane stabilizing action/ quinidine-like / local anesthetic effect• sedative actions / No ISA	
P.K		<ul style="list-style-type: none">• Lipophilic• Completely absorbed• 70% destroyed during 1st pass hepatic metabolism• 90-95% protein bound• Cross BBB and excreted in urine.• Can be given p.o or parenteral	
Action	General	<ul style="list-style-type: none">• Membrane Stabilization: Block Na channels direct depressant to• myocardium has local anesthetic effect (anti-arrhythmic effects).• β-blocking Effect: (anti-arrhythmic effects).• CNS Effect: Has sedative action ↓ tremors & anxiety used to protect against• social anxiety performance anxiety.	
	B1	<ul style="list-style-type: none">• Heart by blocking β_1 :• Inhibit heart properties ↓ cardiac output.• Has anti-ischemic action ↓ cardiac work & ↓ O2 consumption.• Has anti-arrhythmic effects ↓ excitability, ↓ automaticity & ↓ conductivity• by membrane stabilizing activity.	
	B2	<ul style="list-style-type: none">• Blood Vessels: Vasoconstriction ↓ blood flow specially to muscles, other• organs except brain causing cold extremities. • Bronchi: Bronchospasm specially in susceptible patients.• Intestine: ↑ Intestinal motility.• •Metabolism:• liver: ↓ Glycogenolysis → Hypoglycemia adipocytes: ↓ Lipolysis• pancreas: ↓ Glucagon secretion skeletal muscles: ↓ glycolysis• peripheral & central nervous systems: local anesthetic effect ↓ tremors &• ↓ anxiety.	
	B1&B2	<ul style="list-style-type: none">• Has antihypertensive action by:• Inhibiting heart properties → ↓ cardiac output• β blockade: ↓ renin & RAAS system• Presynaptic inhibition of NE release from adrenergic nerves• Inhibiting sympathetic outflow in CNS	
	Indication	<ul style="list-style-type: none">• Chronic glaucoma• Myocardial infarction• Migraine [Prophylaxis]• Angina	<ul style="list-style-type: none">• Pheochromocytoma; used with α-blockers (never alone)• Anxiety: (especially social & performance type)

Nonselective Blocks $\alpha 1$ & β

	Labetalol	Carvedilol
MOA	<ul style="list-style-type: none"> • Rapid acting, non-selective with ISA local anesthetic effect • Given p.o and i.v. • Does not alter serum lipids or blood glucose. • Produce peripheral vasodilation. Due to its action of blocking $\alpha 1$ receptor. • Decrease blood pressure. 	<ul style="list-style-type: none"> • Non-selective with no ISA & no local anesthetic effect. • Has ANTIOXIDANT action
USES	<ul style="list-style-type: none"> • Severe hypertension in pheochromocytoma • Hypertensive crisis (e.g., during abrupt withdrawal of clonidine). • pregnancy-induced hypertension 	<p>CONGESTIVE HEART FAILURE to reverses its pathophysiological changes.</p>
ADRs	<ul style="list-style-type: none"> • Orthostatic hypotension • sedation & dizziness 	<ul style="list-style-type: none"> • Orthostatic hypotension • Edema

Mnemonics (only for drugs mentioned in this lecture):

All β -blockers end in "olol" except mixed blockers \rightarrow end in "lol" only.

All cardioselective β -blockers begin with the letters A \rightarrow M "Exclusive Beta Blockers Are Acting Mainly Cardioselectively" \rightarrow thanks to Abdullah Alomran!

All non-selective β -blockers begin with the letters O \rightarrow Z ($\beta 2$ = second half of the alphabet).

-Mnemonic: "**CO**ntain **P**artial **A**gonistic **A**ctivity": Celiprolol + Oxprenolol + Pindolol + Acebutolol

-Extra note: Beta-blockers with ISA may not be as effective as the pure antagonists in the secondary prevention of MI. They cause less bradycardia & less peripheral vasoconstriction. However, this may be useful in patients who develop symptomatic bradycardia or bronchoconstriction in response to beta-blockers, which makes ISA favorable in particular cases.

-Never use ISA drugs with angina, arrhythmia, & myocardial infarction (we do not want any simple stimulation).





Summaries



β -receptor blockers

Drug	Selectivity	Uses
Propranolol	Nonselective B1&B2 blocker	<ul style="list-style-type: none">• Migraine prophylaxis• Hyperthyroidism (thyrotoxicosis)• Relieve anxiety (social performance)• Hypertension- Arrhythmias• Angina - Myocardial infarction• Pheochromocytoma; used with α-blockers (never alone)• Chronic glaucoma - Tremors
Timolol	B1 B2 blocker	Glaucoma
Atenolol-Bisoprolol Metoprolol	B1 blocker	Myocardial infarction Hypertension
Esmolol	B1 blocker, given IV Ultra short acting	Cardiac arrhythmia
Carvedilol	α , B blocker	Congestive heart failure
Labetalol	α , B blocker	Hypertension in pregnancy Hypertensive emergency

“ study smarter , not harder “

Active recall



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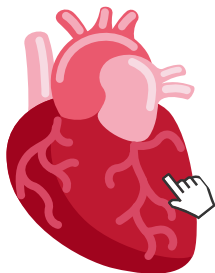


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summary



MCQs

1

Which one of these beta adrenergic blockers is mainly used to treat glaucoma as an eye drop?

A

Atenolol

B

Sotalol

C

Labetalol

D

Timolol

2

A patient was suffering from pheochromocytoma, his physician prescribed him alpha and beta blocker drugs, Explain why he gave him a beta blocker.

A

Lowers the elevated BP

B

Increases BP

C

Protect the heart from NE

D

B & C

3

Which one of these beta adrenergic blockers has the fastest onset of action (10min) and is given IV?

A

Esmolol

B

Bisoprolol

C

Carvedilol

D

Propranolol

4

Which of the following is a Mixed α , β Receptors Blocker

A

Bisoprolol

B

Esmolol

C

Carvedilol

D

Atenolol

MCQs

5

Which ONE of the following is a vasodilating beta blocker that has antioxidant activity?

A

Labetol

B

Propranolol

C

Atenolol

D

Carvedilol

6

What is the suitable drug to use in atrial tachycardia caused by thyrotoxicosis?

A

Quinidine

B

Esmolol

C

Amiodarone

D

Lidocaine

7

An asthmatic hypertensive patient. The physician decided to give him Beta blockers. Which of the following is correct?

A

Beta blockers selective in nature

B

Beta blockers sedative in nature

C

Beta blockers with non-selective activity

D

None of the above



Most Important questions in this lecture!

MCQs

8

One of the following drugs used is in the prophylaxis of migraine:

A

Labetol

B

Propranolol

C

Atenolol

D

Carvedilol

9

Which of the following Beta blockers act as anxiolytic:

A

Propranolol

B

Esmolol

C

Quinidine

D

Lidocaine

10

The beta-blocker which is used in Hyperthyroidism is:

A

Atenolol

B

Quinidine

C

Propranolol

D

Amiodarone

8-B, 9-A, 10-C

MCQs

11

A 50-year-old male was brought to the emergency room after being stung by a hornet. The patient was found to be in anaphylactic shock, and the medical team tried to reverse the bronchoconstriction and hypotension using epinephrine. However, the patient did not fully respond to the epinephrine treatment. The patient's wife mentioned that he is taking a prescription **medication for his blood pressure**, the name of which she does not remember. Which of the following medications is he most likely taking that could have prevented the effects of epinephrine?



A

Doxazosin

B

Propranolol

C

Metoprolol

D

Acebutolol

12

Which of the following patients would not benefit from beta blockers?

A

64-year-old female with daily migraines

B

57-year-old male with past history of coronary artery disease

C

56-year-old male with erectile dysfunction

D

74-year-old male with history of systolic heart failure that is stable

SAQs

1

list 5 of the clinical uses of beta receptor blockers:

Answer:
Pheochromocytoma
Arrhythmia
Hypertension
Myocardial infraction
Glaucoma



2

How are beta blockers perform Antianginal effects (in treating ischemic heart disease) ?

Answer:
By ↑ Heart rate
(bradycardia), ↑ force of contraction cardiac work, and ↑ Oxygen consumption due to bradycardia .



3

What are the uses of Labetalol?

Severe hypertension in

- pheochromocytoma
- Hypertensive crisis (e.g., during abrupt withdrawal of clonidine),
- pregnancy-induced hypertension

slide14



SAQs


4

list 5 ADRs of b-blockers

- ◆
- Answer:
- Depression, hallucinations, Fatigue
 - Gastrointestinal disturbances, Sodium retention
 - hypoglycaemic manifestations in diabetic patients i.e. tachycardia, sweating → COMA.
- slide 11

5

What are the uses of Propranolol?

- ◆
- Answer:
- Migraine prophylaxis
 - Hypertrophic cardiomyopathy (hypertrochosis)
 - Relieve anxiety (social performance)
 - Hypertension- arrhythmias
- Slide 13
- 



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