Pharmacology Team

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Red	Important
Purple	Extra Notes
Orange	General Explanation
Black	From the slides
Green	From male

كل الادوية تنتهي ب LO

- Adrenoceptor Blockers

Pharmacodynamic

According to extent of blocked of each type they are either

Non-Selective

Block 1 & 2
Propranolol, Timolol, Pindolol

Block & a_1
Labetalol, Carvedilol

Selective

Block 1 >> 2
Atenolol, Bisoprolol, Metoprolol

According to presence of agonistic /antagonistic action* (ISA) = PARTIAL AGONISTS or only antagonistic

With ISA

Labetalol

Without ISA

Propranolol, Timolol, Atenolol, Bisoprolol, **Carvedilol**

Pharmacokinetic Classification

According to their lipid solubility

	Lipophylic	Hydrophilic
Oral absorption	**Complete**	**Irregular**
Liver metabolism	**Yes**	**No**
Half life	**Short**	**Long**
CNS side effects	**High**	**low**
	Propranolol, Pindolol, Timolol. Metoprolol Labetalol > Carvedilol	**Atenolol, Bisoprolol**

***ISA= Intrinsic Sympathetic Activity, It means that while the drug is blocking -receptor, it can also act as agonist and gives a little sympathetic effect.**

Kinetics

1- Completely absorbed

2- 70% destroyed during 1st pass hepatic metabolism, "because of that, we have to increase the oral dose"

3- 90-95% protein bound, "it may cause drug-drug interaction"

4- Cross BBB

Dynamics

1. Non-Selective Blocker of $_1$ & $_2$

2. Has membrane stabilizing action "Inhibition of action potentials from being propagated across the membrane. Membrane stabilization is the method through which local anesthetics work. This effect is similar to the membrane stabilizing activity of sodium-channels blockers that represent Class I antiarrhythmics. "

3. Has sedative action "because it is cross BBB"

Actions

Site of effect	Type of receptor	Action
Heart	block $_1$	1- Inhibit heart properties (inotropic, chronotropic, dromotropic & lusiotropic) cardiac output 2- Has anti -ischemic action cardiac work + O_2 consumption "O_2 supply which provided to the heart is enough to keep it protected from ischemia" 3- Has anti-arrhythmic effects excitability, automaticity & conductivity + by membrane stabilizing activity
BP	block $_1$ & $_2$	1- Has antihypertensive action by : Kidney ↓ renin & aldosterone secretion (β1). (Very important). - Vasoconstriction to kidney BV " blocking RAAS system" - Presynaptic inhibition of NE releases from adrenergic nerves "2-receptors, which located in presynaptic part, are responsible for releasing NE. So, if we block it, NE release will be reduced". - Inhibiting sympathetic outflow in CNS
Blood Vessels [BV];	block $_2$	Vasoconstriction blood flow to all organs cold extremities + (intermittent claudications) "because the muscle has no good supply of blood". **(Therefore, it is contraindicated in peripheral diseases like *Raynaud's disease*)**
Bronchi	block $_2$	Bronchospasm
Intestine	block $_2$	Intestinal motility colics

Metabolism:	block mainly $_2$	In liver; Glycogenolysis Hypoglycemia In pancreas; Glucagon secretion In adipocytes; Lipolysis In skeletal muscles; glycolysis Hyperkalemia
On peripheral & central nervous systems		Has local anesthetic effect tremors & anxiety مثل لمن يكون عندهم رهبة الالقاء في المؤتمرات ، محاضرات " "

INDICATIONS

1- Hypertension

2- Arrhythmias; Ventricular > atrial

3- Angina

4- Myocardial infarction infarct size Cardioprotectivedeath

If the myocardial infarction was massive it could lead to a cardiogenic shock. في هذي المرحلة عادة ما نقدر نعطي المريض بيتا بلوكرز

- ↓ myocardial O_2 demand.
- ↑ Redistribution of blood flow in the myocardium.
- free fatty acids.
- Anti-arrhythmic action.
- incidence of sudden death

Not important, but better to know.

5- Migraine [*Prophylaxis*]

6- Pheochromocytoma "NE sever tachycardia -blockers to protect the heart"; used with -blockers (never alone).**

"We use -blockers to decrease BP"

7- Chronic glaucoma; IOP by secretion of aqueous humor

8- Tremors

9- Anxiety; *(specially social & performance type)*

10- Hyperthyroidism "sympathetic over activity";

- Controls tachycardia, tremors, sweating
- Protects heart against sympathetic over-stimulation.
- Lowers conversion rate of T4 into T3

"thyroid hormones, triiodothyronine (T_3) and thyroxine (T_4)"

** A **pheochromocytoma** is a neuroendocrine tumor of the medulla of the adrenal glands , secretes high amounts of catecholamines, usually noradrenaline (norepinephrine), and adrenaline (epinephrine).

ADR

Due to block of cardiac $_1$- receptors:

- Heart failure
- Bradycardia ***treated by atropine***
- Hypotension

- Depression, nightmares, vivid dreams and hallucinations. "Drugs that cross BBB"
- Gastrointestinal disturbances.
- Sodium retention
- Hypersensitivity reactions

Due to blockade of $_2$- receptor: ***(only with non-selective b-blockers)***

- Asthma, emphysema, chronic bronchitis
- Cold extremities & intermittent claudication
- Erectile dysfunction & impotence "we don't give it to a male in fertility age "
- Hypoglycemia & triglycerides

Diabetic patient:

- **All -blockers mask (تخفي) hypo-glycaemic manifestations develop COMA "When diabetic patient has hypoglycemia, his body will translate this condition as stress sympathetic over activity. So, if he takes -blockers he will not feel hypoglycemia, and he may develop coma."**
- **If we need to give -blockers to diabetic patient! We have to give him Selective 1-blocker. (Atenolol,bisoprolol)**

At the end of treatment

- Selective: **Only ($_1$)**: Safer in:
Asthma / Diabetes & Dyslipidemias
Rauynald's phenomenon & vascular diseases.

- Sudden stoppage will give rise to withdrawal manifestations:

Rebound angina, arrhythmia, myocardial infarction & hypertension.

WHY? Up-regulation of -receptors.

- So drug must be withdrawn gradually To prevent withdrawal manifestations

BUT..

With ISA (**Partial agonist**), complication will be less.

Better in patients that exhibit excessive bradycardia

Also in non compliant for fear of sudden stoppage

Not useful in patients with AMI(acute myocardial Infarction), angina & tachyarrhythmias

Contraindications

- **Depressed myocardial** → عشان كذا لو كان التوتر مرضي و ليس مؤقت ما نعطيهم لأن الاستخدام المطول لها ممكن يؤدي للاكتئاب .
- **Hypotension**
- **Bronchial Asthma**
- **Peripheral vascular**
- **Diabetic patients**

Pharmacodynamic Interactions

DRUG	IF we use it with -blockers
verapamil	both induce A.V block
cocaine, amphetamine or a-blocker overdose " if we use -blockers as treatment of hypertension, that has developed due to using of cocaine, amphetamine"	Rebound hypertension
NSAIDs	Increase the dose. " if we use -blockers as anti-hypertensive"
Quinidine (cardiac depressants)	Heart failure
Ergot (in migraine)	Claudications
Tubocurarine (neuromuscular blocker)	Enhanced neuromuscular blockade
Anti-diabetic	Hypoglycemia (Non selective -blockers)

Blocks & $_1$ (Another name: **vasodialating -blockers)**

Used in 1- Severe hypertension in pheochromocytoma & hypertensive crisis (eg: during abrupt withdraw of clonidine)

2- May be used pregnancy-induced hypertension but better methyldopa.

Blocks > $_1$ (so more vasodialating)

Has antioxidant action. Used effective in congestive heart failure

summary.

- Agents specifically indicated for hypertension

Atenolol, Bisoprolol > Metoprolol, Propranolol

- Agents specifically indicated for cardiac arrhythmia

Propranolol > Atenolol Esmolol Sotalol

- Agents specifically indicated for congestive heart failure

Carvedilol, Bisoprolol, Metoprolol

- Agents specifically indicated for myocardial infarction

Atenolol, Metoprolol, Propranolol

- Agents specifically indicated for glaucoma

Timolol

- Agents specifically indicated for migraine prophylaxis

Timolol, Propranolol

Questions

1- A 38 year old male has recently started monotherapy for mild hypertension. At his most recent office visit, he complains of tiredness and not being able to complete three sets of tennis. Which one of the following drugs is he most likely to be taking for hypertension ?

A- Albuterol.
B-Atenlolo.
C-Ephedrine.
D- Prazosin.

2- If we have to give beta blockers to a diabetic patient, which one of these drugs is suitable :
A- Propranolol
B-Atenolol
C-Rimolol
D- Pindolol

3- Cold extremities is a side effect that appears due to blocking of :
A- Beta1-receptors.
B-Alfa1-receptors.
C-Alfa2-receptors.
D- Beta2-receptors.

4- Which one of these drugs is suitable in patients that exhibit excessive bradycardia :

A- Bisoprolol.
B-Carvedilol.
C-Lebetalol.
D- Timolol.

5- Which one of these drugs is appropriate to use in the case of pregnancy induced hypertension :
A- Carvedilol.
B-Labetalol.
C-Atenolol.
D- Pindolol.

6- Which one of these drugs is affective in cases of congestive heart failure :
A- Labetalol.
B-Atenolol.
C-Metoprolol.
D- Carvedilol.

Answers

1	B
2	B
3	D
4	C
5	B
6	D