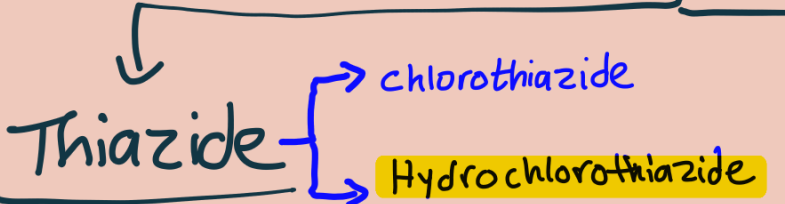


Antihypertensive Therapy

Diuretics



↓ Na⁺ body stores
 ↑ urinary Na⁺ & water excretion

- Initially, diuretics reduce blood pressure by reducing blood volume and cardiac output; peripheral vascular resistance may increase. *الضغط الوريدي ما ينزل*
- After 6-8 weeks, cardiac output returns toward normal while peripheral vascular resistance declines. *الضغط الوريدي ما ينزل*

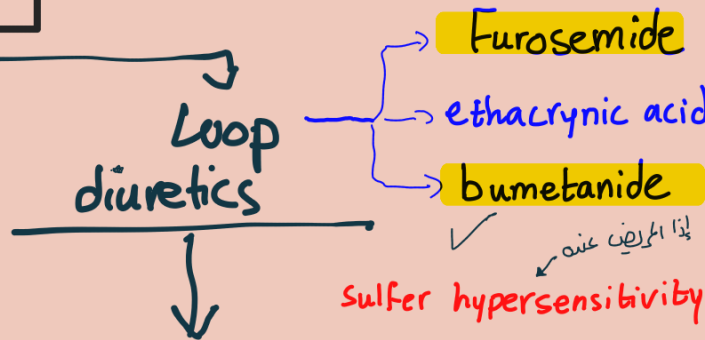
lower doses (25-50 mg) exert as much antihypertensive effect as do higher doses.

يعني ما في داعي تزيد الـ Dose لأنه على الجهاين
 مع يعطى نفس الـ effect

* Adverse effects

- hypokalemia → *مس كلى بتبين
إلديزا كان ياخذ digoxin*
- hyperurecemia → inhibition of renal tubular secretion of uric acid
- hypercalcemia
- hyperglycemia (قليل)

* لازم المريض يقلل dietary Na⁺ intake



produce greater diureses than thiazides, but they have weaker anti-hypertensive effect and cause severe electrolyte imbalance.

* For renal failure ✓

- Typically only beneficial in patients with
 - resistant HTN and evidence of fluid; *edema*
 - effective if CrCl < 30 ml/min
- MUST be dosed at least twice daily (Lasix = Lasts six hours)
- Administer AM and lunch time to avoid nocturia

* Adverse effects

- hyperurecemia
- hypocalcemia
- Ototoxicity Type B Adverse effect [Not Dose dependent]
*يعني هاي الـ Toxicity بتغير على أي Dose
 مس مرتبطة بالـ high Dose بس*

Specially with

- Aminoglycosides
- Cisplatin

↑ مع هدول Loop diuretic
 يمنع ياخذ

stage drugs

β - blockers

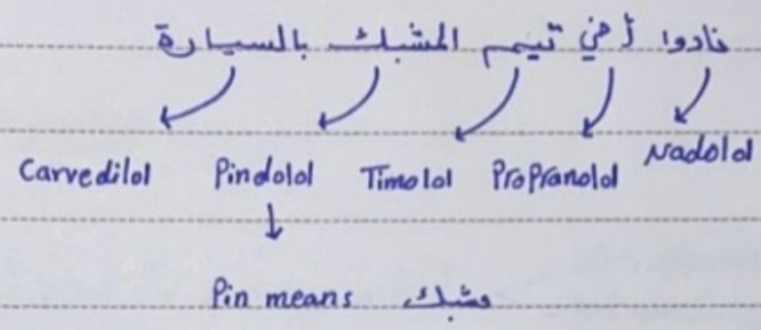
For Congestive heart failure lower doses

For Angina higher doses

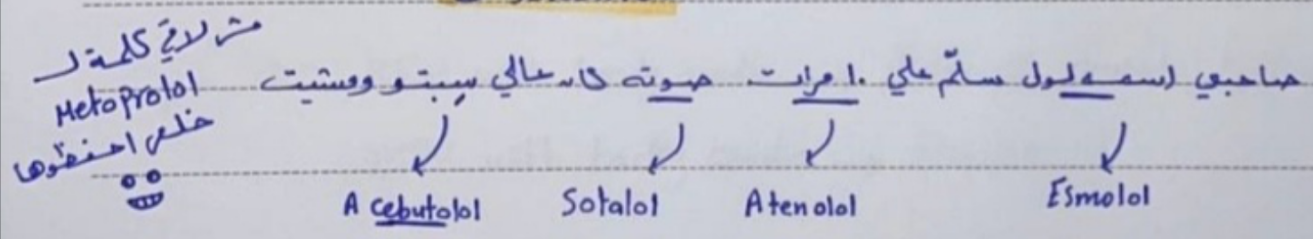
Fatigue يعني

2 Types

① Non selective :



② Selective :



منفع نفسي Non-selective

• * Non selective β blockers \rightarrow Adversely affect patients with asthma < DM

α_1 β_1 β_2 \leftarrow Carvedilol & Labetalol \rightarrow Used in Pheochromocytoma HTN or emergency HTN

intrinsic sympathomimetic activity \leftarrow Pindolol & Acebutolol & Penbutolol \rightarrow Partial agonists (used to treat patients with)
 peripheral vascular disease \leftarrow HTN \leftarrow Bradycardia
 peripheral Dilation

• * Sotalol \rightarrow Anti-arrhythmic (prevent & treat arrhythmias)
 + Propranolol
 • Esmolol \rightarrow work fast, end fast / used in emergency HTN

Titration

* Metoprolol & atenolol → most widely used blockers (HTN)

* Labetalol & carvedilol → both example β & α blockers.

3rd line therapy for managing HTN in Pregnancy

* Esmolol → ① Used for management to < intra operative HTN
post operative
② emergencies, when HTN associated with (Tachycardia)

*** So: HTN with brady cardia → Pindolol, acebutolol, penbutolol
HTN with tachy cardia → Esmolol

*** Sudden withdrawal may cause Rebound HTN
tachycardia / tachy arrhythmia also happen after this sudden withdrawal

*** The withdrawal syndrome may involve ↑ up-regulation or supersensitivity of β receptor adrenoceptors.
→ so the removal of β blocker should be gradual

- * Timolol → treating glaucoma.
- * Pilocarpine → treating acute glaucoma.

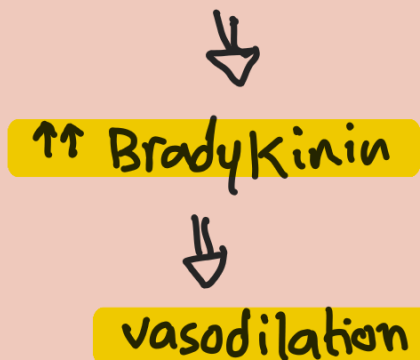
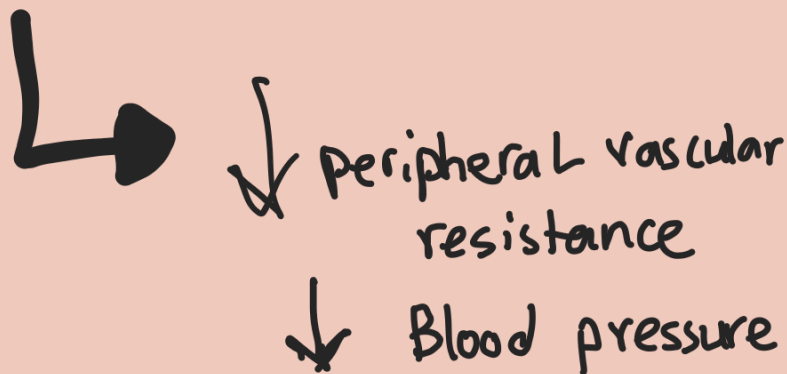
pril

ACE inhibitors

Blocks Angiotensin converting enzyme

Blocks the synthesis of Angiotensin II

Blocks the breakdown of Bradykinin



* side effects

- Dry cough
- hyperkalemia
- Angioedema — rare
- Risk of first-dose syncope

Can be used in chronic kidney disease & Diabetes even there is No hypertension

Contraindicated in pregnancy
Bilateral renal stenosis

Note

ACEIs Not 1st line therapy in Blacks
Chronic kidney disease or Diabetes

... Sartan

ARBs

angiotensin II - receptors
blockers

- Their pharmacologic effects are **Similar to ACE Inhibitors** (vasodilation, block aldosterone secretion), however they **do not increase the baradykinin levels.**
- Their adverse effect are similar to ACE Inhibitor, although the risks of cough and angioedema are significantly decreased. **Hyperkalemia**

Fetal renal Toxicity

السبب

↓ Aldosterone

↓
K⁺ accumulation

Absolute contraindication in pregnancy

relative contraindication with ACEIs

يعني لا ACEIs & ARBs مع بعض
إلا بحالة واحدة (نادرة جداً)

in patient with heart failure

and Dose Not respond to any drug

← يعني الحالة ببغيتي ← ARBs & receptor blocking

← ACEI يعني synthesis

fatigue تعب

Ca⁺⁺ channel blockers

The most effective drugs within the 1st line therapy
 1st line therapy in Blacks —

ACEI ← Diabetes or Chronic kidney disease
 يأخذ ACEI

They exerts their antihypertensive effect by their **vasodilation** effect.

side effects لازم نراقب

- reflux Tachycardia
- Na⁺ & water retention
- Edema
- headach

effect by antagonists block for the inward movement of calcium by binding to the **L-type channels** in the heart and peripheral vasculature.

Dilation

AV node SA node
 -ve chronotropic
 myocytes
 -ve inotropic

with very little binding to the hearts
 selective to L-type c⁺⁺ channel in vessels

	NIFEDIPINE*	DILTIAZEM	VERAPAMIL
coronary arteries dill	++	++	++
peripheral arteries dill	++++	++	+++
negative inotropic	⊕	++	+++
slowing AV cond	↔	+++	++++
heart rate	↑ ↔	↓ ↔	↓ ↔
↓ blood presure	++++	++	+++
depression of SA	↔	++	++
increase in cardiac output	++	↔	↔

reflux tachycardia or palpitation

moderate

Adverse effects of calcium channel-blocking agents

sustain release once daily
تفريغ
AE

نصف عمر
short acting
half life

Advers effects
تكون آثار

Drug	Effect on heart rate	Adverse effects
Nifedipine	↑	Headache, flushing, ankle swelling
Amlodipine	↑	Ankle swelling
Nimodipine	±	Flushing, headache
Diltiazem	±	Generally mild
Verapamil	↓	Constipation, marked negative inotropic action

gingival hyperplasia
thickening of gingiva

Postural hypotension

cross BBB vasodilation in Brain [Brain selective]

Calcium channel blockers **do not affect** concentrations of plasma cholesterol or triglycerides, or extracellular calcium homeostasis.

reflux Tachycardia
C-max
تسرع

دواء
doxazosin
silodosin

Selective α_1 - blockers

- Used in the treatment of chronic hypertension
- Also used to treat urinary retention in men with benign prostatic hyperplasia

side effects
لازم نراقب

- reflux Tachycardia
- Na^+ & water retention
- 1st dose syncope

Centrally acting adrenergic drugs

Clonidine

α_2 agonist

desensitization
(↓ No. of receptors)

useful in hypertension
with renal disease

↓ heart rate }
↓ cardiac output } ميثيل دوبا methyl dopa

* side effects

- dry mouth
- sedation

زى مين؟؟ β -Blockers

● withdrawal of clonidine
after protracted use
with high doses

↳ threatening hypertensive crisis

stopping should be Gradually

Methyldopa

weak α_2 agonist

weak Anti-hypertensive

* main effect

diminish the
adrenergic outflow
from the
CNS

↓ Norepinephrine

Valuable in

hypertension with
renal insufficiency

renal dilation تبعيل

hypertension during

pregnancy

* side effects

sedation

drowsiness

Vasodilators

Smooth muscle relaxants

Hydralazine

Arterial dilation

intracellular Ca^{++} blocking

side effects

Na^+ & water retention

⊕ β -blocker
Thiazide

reflux
Tachycardia

⊕ β -blocker

Lupus-Like Syndrome

⚡ with high doses

+ يزيد اصقلية
when > 6 months therapy

in females
in whites
Better to use

in males

+ Blacks

nitroprusside

Veins + Arteries dilation

- relaxation of smooth muscles by

↑ NO

↑ cGMP
dephosphorylation of myosin

بشغل بسرعة

بنتقى بسرعة

Good for

⊗ emergency hypertension

side effects

Cyanid thio toxicity

↓

lactic Acidosis

fendopam

Arterial dilation

- Dopamine-1 receptor agonist

بشغل بسرعة
ببنا ببطري بسرعة

uses

emergency

⊗ Kidney dilation

↪ Dopamine receptors along the

nephron

promoting

Na^+ excretion

minoxidil

Arterial dilation

- relaxation of smooth muscles by K^+ efflux

⊕ β -blocker
Loop Diuretic

side effects

hypertrichosis

* less preferred in females

- They produce reflex stimulation of the heart resulting in increasing the myocardial contractibility, heart rate, and oxygen consumption, so they may prompt angina, Myocardial Infarction in predisposed individuals .
- They increase plasma renin concentration, which resulting in sodium and water retention.
- These unwanted effects can be blocked by the combination with a diuretics and a β blocker.
- **Hydralazine monotherapy is accepted method of controlling blood pressure in pregnancy-induced hypertension.**

Hypertension emergency

1st choice \Rightarrow Sodium nitroprusside

then

Fenoldopam

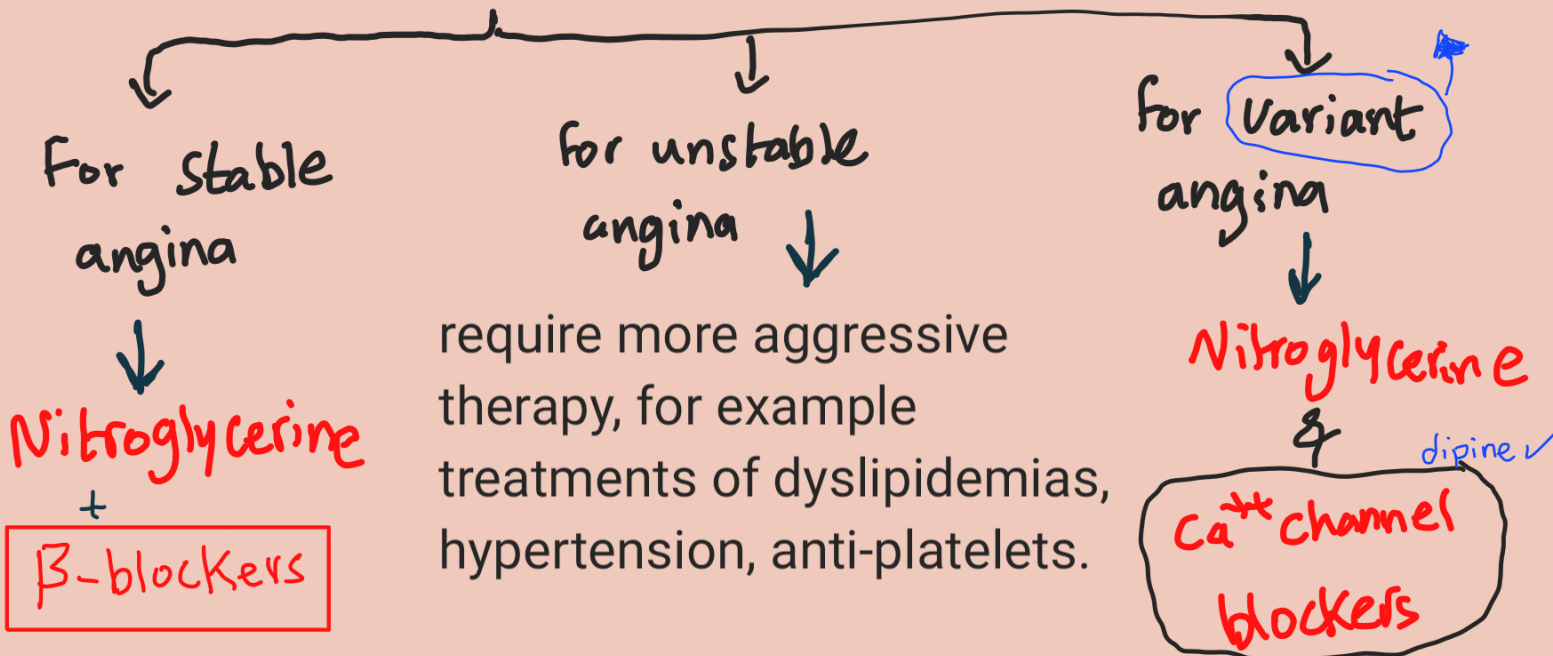
then

Lapitolol

Non-selective
contraindication \Rightarrow Asthma

Anti-Anginal Drugs

Contraindication with β-Blocker عقار



organic Nitrates

Nitroglycerine

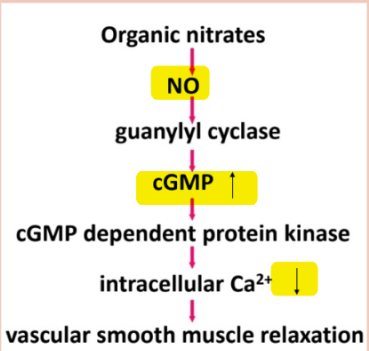
Sublingual
Transdermally (patch)

orally

100% 1st pass metabolism

isosorbide dinitrate
mononitrate

complete 1st pass metabolism orally ✓



- Decreased ventricular volume
- Decreased arterial pressure
- Decreased ejection time
- ↓ O₂ requirements
- Vasodilation of epicardial coronary arteries
- Increased collateral flow
- Decreased left ventricular diastolic pressure

contraindication with **Sildenafil** ((Viagra)) الحبة الزرقاء

⊖ phosphodiesterase ↑ cGMP

Postural hypotension Syncope

orthostatic hypotension

reflux Tachycardia

↓ diastolic perfusion time

Side effects →

Syncope

Throbbing headache

↳ ↓ After first few days [tolerance]

we give Nitrates + β-blockers ✓

or Ca⁺⁺ blockers

Verapamil ✓
Diltiazem ✓
dipine X

Tolerance

عابدينا يهبر

- Tolerance to the action of the nitrates develops rapidly, the blood vessels become desensitized to the vasodilation.
- Why????? diminished release of nitric oxide resulting from depletion of tissue thiol compounds may be partly responsible for tolerance to nitroglycerin.
- The tolerance can be overcome by providing a daily "nitrate free intervals" to restore sensitivity to the drug (this interval are usually 10 - 12 hr at night)

صبة لصبح
صبة الفصح



Important notes to your patient

- The conventional sublingual tablet form of nitroglycerin may lose potency when stored as a result of volatilization and adsorption to plastic surfaces. Therefore, it should be kept in tightly closed glass containers. Nitroglycerin is not sensitive to light.
- spray is equally effective; it has a shelf life of two to three years and does not require refrigeration

بغيرها
شهر

Nitrates

side effects

reflex Tachycardia

↓ diastolic perfusion time



↓ myocardial O₂ requirement

β-blockers

side effects

↑ end-diastolic volume

↑ ejection time



↑ myocardial O₂ requirement

Both balance each other

Newer Antianginal drugs

Ivabradine

closes Na^+ channels

selectively inhibits the **If current**

important current involved in generating the **early phase** of spontaneous diastolic depolarization in sinoatrial cells

effect on **SA node**

reducing the **frequency of action potential** initiation and **lowering heart rate**.

reduces slope of depolarization

-ve chronotropic

↓ myocardial O_2 demand

metabolised by **CYP3A4**

It is **contraindicated** to be used with **verapamil** and **diltiazem**.

• Used in **HF** with β -blockers

with **LVEF < 35%**

↓ risk of hospitalization for HF

Adverse effects

• **Luminous phenomena**

sensations of enhanced **brightness** in a fully maintained visual field due to blockage of **Ih ion channels** in the retina

Bradycardia

Ranolazine

selectively inhibits the **late sodium influx** in the myocardium, **reducing calcium overload**

attenuating the **ischaemic abnormalities**

Cardiac stiffness

↓ diastolic tension

No effect on HR or BP

↓ O_2 demand

contraindication in patients with **mild-severe Liver disease**

Adverse effects

• **↑ QT interval**

the result of **inhibition** of **IKr**, which prolongs the ventricular action potential.

Trimetazidine

metabolic Drug

Switcher of energy production from

Fatty Acids → **Glucose metabolism**

⊖ **CPT1**

⊖ **β -oxidation**

Inhibition of the reduction of adenosine triphosphate (ATP) stimulation of glucose consumption by the myocardium

No effect on HR/BP **chronotropic inotropic**

↓ O_2 demand

Contraindication

Parkinson's disease

Adverse effects

parkinson

• **Extrapyramidal**

• **Restless leg Syndrome**

Nicorandil

2 parts

Nitrate يشغل on K^+ level

• It increases **cyclic guanosine monophosphate** and facilitates the opening of **mitochondrial potassium adenosine triphosphate channels**.

second-line option to treat patients with **stable angina**

Adverse effects

GI, Skin, mucosal

• **Ulceration**

Drugs used in HF

- (1) ACE inhibitors,
- (2) β -adrenergic blocking agents,
- (3) diuretics,
- (4) **inotropic agents**,
- (5) direct vasodilators, and
- (6) **aldosterone antagonist**.

Digitalis

→ Acute HF & shock

Spirolactone For HF due to LVSD

side effect

prevent { Na⁺ retention
MI
hypokalemia

hyperkalemia

CNS effects

endocrine abnormalities

gynaecomastia

بىسپىرونولون

سپىرونولون

↓

Eplerenone

⊕ monitoring
K⁺ & creatinine
level

Inotropic Drugs

Digoxin

+ve inotropic
-ve chronotropic

↑ Contractability of heart muscles

↑ Vagus nerve activation
↑ Ach release to M2 receptors of heart
↓ sinus rhythm

Low Therapeutic index

Adverse effects / intoxication

↓ serum K⁺

Anorexia, nausea, vomiting, diarrhea
fatigue, headache

Arrhythmia

● vision changes **xanthopsia**

● Antidote For Digoxin Toxicity

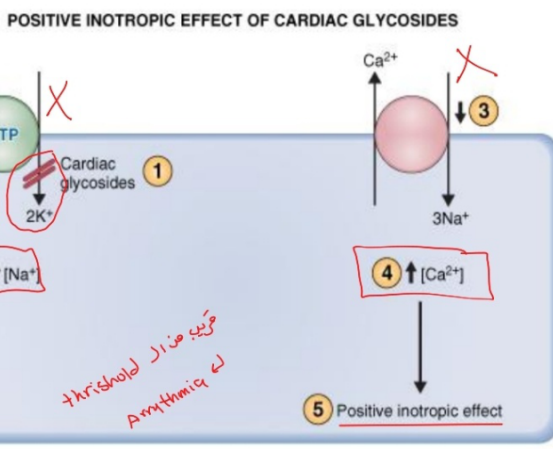
Digifab

Digibind

} monodonal antibody for Digoxin

wolf syndrome

{ Digoxin
 { β-blocker
 { Ca⁺⁺ channel blocker



hypoKalemia لازم نراقب الـ

لونه إذا قل الـ K⁺

الـ Digoxin فارغ يعمل

Competition مع الـ K⁺

بالتالي رفع يتراكم ويعمل toxicity

Digoxin interaction:

Quinidine, verapamil, and amiodarone can cause digoxin intoxication, both by replacing digoxin from tissue protein binding sites, and by competing with digoxin for renal secretion. *

Macrolide and tetracycline antibiotics should be avoided because they elevate digoxin serum concentration and enhance the risk for digoxin toxicity

Digoxin metabolism لا يُؤثر على microbites لا تؤثر *

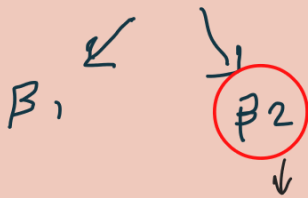
95/

Dobutamine

intravenous

Acute HF in hospital setting

Non-selective β -Agonist



Vasodilation

↓ Blood pressure

also resin

Low level of

Norepinephrine

vassopressor

to ↑ vascular resistance