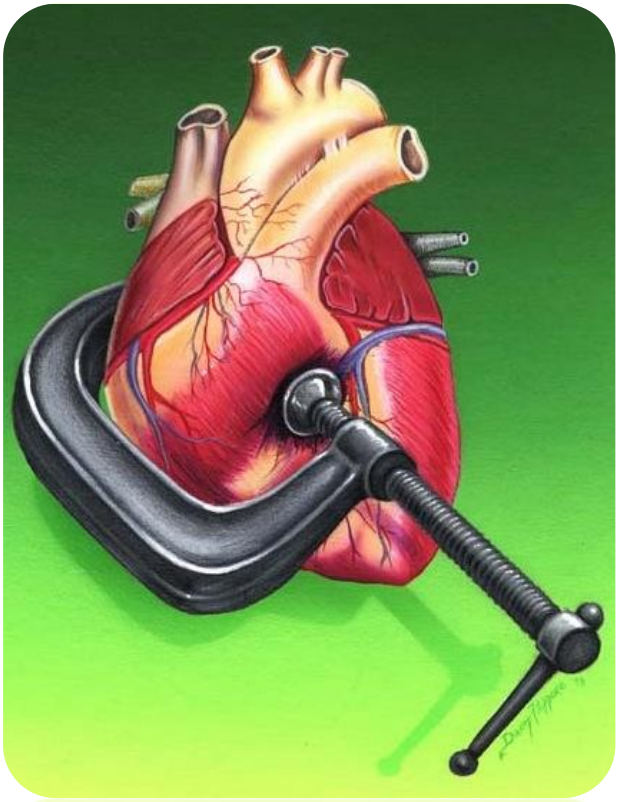
Pharmacology Team
429 Medicine

HYPERTENSION



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HYPERTENSION

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ملاحظة :

المذكرة عبارة عن سلايدات د.عزة بالإضافة إلى نوتات التيم.

Ps: the notes are in orange color or gray squares

الدكتورة قالت مهم نعرف :

في هذا الدرس الدكتورة قالت جدا مهم نعرف الأدوية خصوصاً
جدول Vasodilators

حتى قالت طريقة الأسئلة في الاختبار تكون :
- مباشر
- problem

المباشر: بأن تقول لك مثلا من الأعراض الجانبية لهذا الدواء ... و أنت اختاري
أما المسألة بأن تجيب لك حالة مريض و فيه المرض الفلاني ايش الدواء المناسب .
قالت هذا السؤال لا تخافو منو بس ركزوا وانتو تذاكروا على استخدامات الأدوية ... و أكددت لي انو إن شاء الله ما يطلع من سلايداتها إن شاء الله.
و قالت برضو من ضمن المسائل تعطينا مريض يشكي من مرضين ايش الدواء المناسب له..
و قالت هذا السؤال الهدف منو إن الطالب يفكر.يعني يشغل مخو . و انو هو هذا الهدف من نظامنا الجديد . مو نحفظ و بس .. يبغونا نفهم
لا تخافو سهله إن شاء الله و بإذن الله كلنا راح نعرف نحل .. طبعا أنا قلت لها انو مسألة متعودين .. فاقترحت عليها تعطينا MCQ حيكون صعب علينا و احنى مو
على اساس نتدرب و ما ننفجع يوم الاختبار بسؤال عجيب .. فاعطتني MCQ
و برضو قالت في كتاب Lipncott
حتلاقو خلف كل درس MCQ
قالت قد تفيد مع إنها ما تؤيد اسئلة الكتب
موفقين جميعا و الفارما مادة جميله جدا بس نركز واحنى ندرس

Head Lines :

- Etiology
- Risk factors
- Mechanism
- Complications
- Treatment

Antihypertensive Agents:

- Diuretics
- Drugs acting on sympathetic system
- Direct vasodilators
- Drugs acting on renin-angiotensin aldosterone system
- Calcium channel blockers

DIURETICS:

- Initially they increase sodium & water excretion this cause :

  Reduction in blood volume & C.O.

- Lately : Reduce peripheral resistance

Team Note:

Main Mechanism :

- Reduce Blood Volume & Cardiac output

Lately :

- Vasodilator effect

Clinical uses:

- Are effective alone for mild or moderate essential hypertension.
- In severe hypertension they are given in combination with other antihypertensive agents.

Adrenoceptor –Blocking Agents:

- β- adrenoceptors are used in mild to moderate hypertension.
- In severe cases used in combination with other drugs.
- They lower blood pressure:

  By decreasing cardiac output.

  Inhibiting the release of renin from the kidney.

Team Note:

In Hypertension → increase of sympathetic activity means : HR, C.O , Heart contractility

β - adrenoceptors → reduce sympathetic activity result in C.O

α-Adrenoceptor Blockers:

- They block α- receptors in arterioles and venules.
- More effective when given in combination with β-blockers or diuretics.

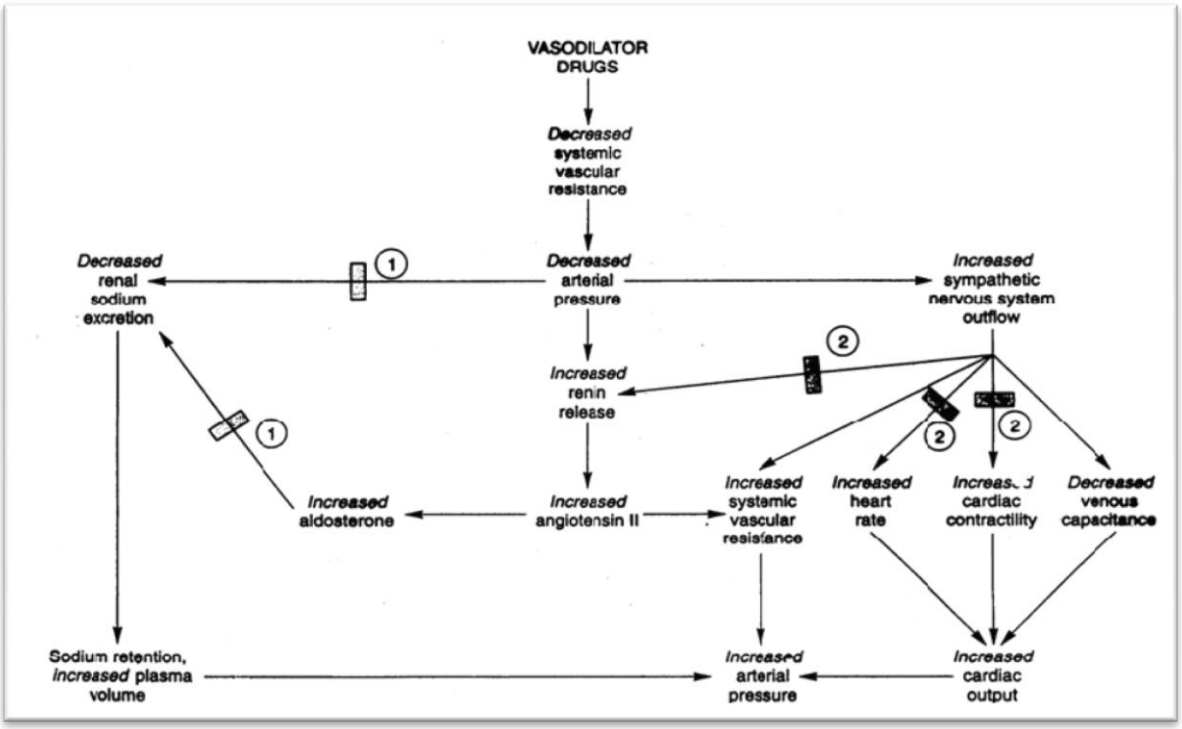
Team Note:

β-blockers >> work on↓ CO + renin

α-blockers >> work on ↓ peripheral resistant

VASODILATORS

Compensatory Response to Vasodilators



Vasodilators

	Hdralazine	Minoxidil	Diazoxide	Na nitropruside
Site of action	Arteriodilator	Arteriodilator	Arteriodilator	**Arterio & venodilator**
Mechanism of action	Direct	Opening of potassium channels in smooth muscle membranes by minoxidil sulfate (active metabolite)	Opening of potassium channels	**Release of nitric oxide (NO)** (It's a potent vasodilator)
Route of admin.	Oral	Oral	Rapid intravenous	**Intravenous infusion**

Continue Vasodilators	**Hdralazine**	**Minoxidil**	**Diazoxide**	**Na nitropruside**
Therapeutic uses	1.Moderate -severe hypertension.	1.Moderate – severe hypertension	1.Hypertensive emergency	1.Hpertensive emergency
	In combination with diuretic & β-blockers			
	2.Hypertensive pregnant woman	2.correction of baldness (لعلاج الصلع)	2.Treatment of hypoglycemia due to insulinoma (cancer of pancreas lead to → insulin)	2.Severe heart failure

Con.Vasodilators	**Hdralazine**	**Minoxidil**	**Diazoxide**	**Na nitropruside**
Adverse effects	Hypotension, reflex tachycardia, palpitation, angina, salt and water retention (edema) **(To avoid side effect : in combin with β-blocker and Diurtic)**			Severe hypotension
Specific adverse effects	lupus erythematosus like syndrome	Hypertrichosis. (excess growth of hear) Contraindicated in females	Inhibit insulin release from β cells of the pancreas causing hyperglycemia Contraindicated in diabetic	1.Methemoglobinduring infusion 2. Cyanide toxicity 3. Thiocyanate toxicity

CALCIUM CHANNEL BLOCKERS:

- Inhibit calcium influx **(there will be relaxation)**

into arterial smooth muscles and cardiac tissues.

- Classified into:

1-Dihydropyridine group (ex.:**nifedipine**) is more selective as vasodilator than a cardiac depressant.

2-Verapamil is more effective as cardiac depressant.

3- Diltiazem has intermediate effect.

Clinical uses

- Treatment of mild to moderate essential hypertension

Team Note:

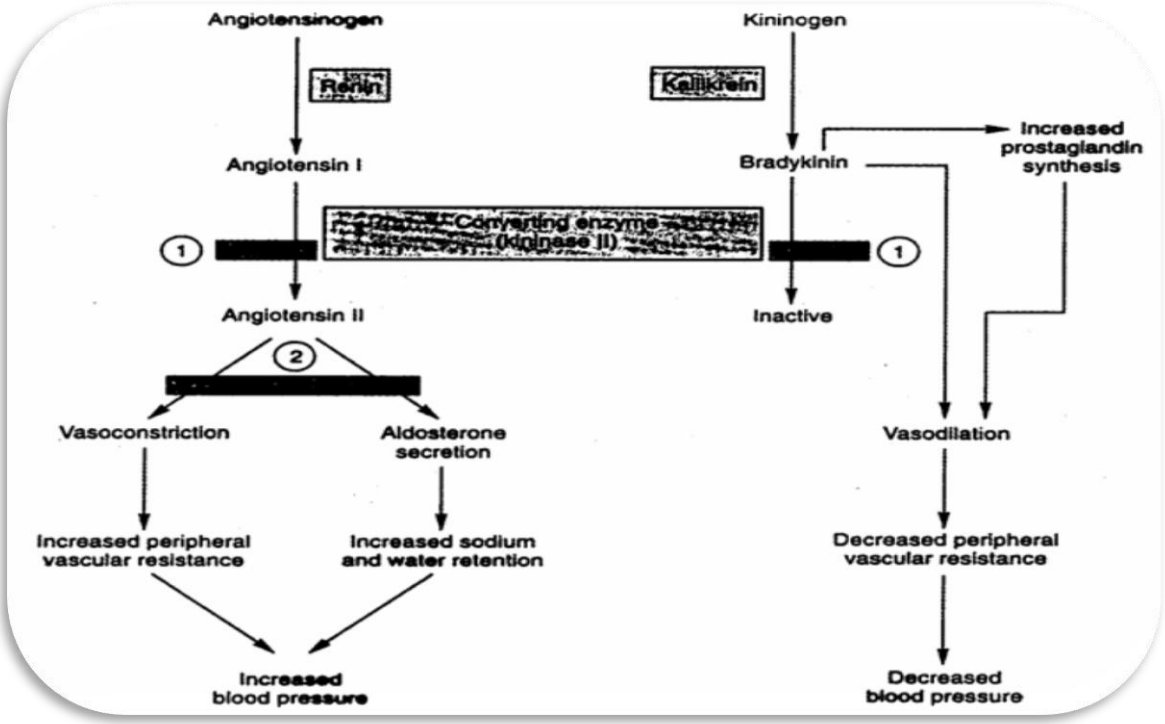
CALCIUM CHANNEL BLOCKERS :

	site of action	therapeutic use	mechanism
Dihydropyridine group nifedipine	Vasodilator selective	mild to moderate essential hypertension	Inhibit calcium influx into arterial smooth muscles and cardiac tissues.
Verapamil	Cardiac selective		
Diltiazem	Cardiac selective		

Angiotensin Converting Enzyme Inhibitors (ACEI)

- Inhibition of ACE leads to:
  - Inhibition the synthesis of angiotensin II.
  - The stimulation of Kallikrein-Kinin system.

Sites of action of ACE inhibitors & Receptor blockers



ACEI Characteristics:

- Unlike vasodilators ; no reflex sympathetic activation; so they can be used safely in patients with ischemic heart disease.

Pharmacokinetics:

- Captopril, enalapril and ramipril .
- All are rapidly absorbed from GIT after oral administration.
- Food reduce their bioavailability.
- All are prodrugs,converted to the active metabolite in the liver (Except Captopril).
- Captopril has a short half-life ,taken 2-3 times daily.

Phrmacokinetics:

- The other drugs have long half-life.
- Enalaprilat is the active metabolite of enalapril is available only for intravenous use for hypertensive emergency.
- All ACEI are distributed to all tissues except CNS.

Team Note: **We have 3 drugs for Emergency patient :**

1- ACEI→ ex:enalapril
2- vasodilators→ ex :Na nitropruside + Diazoxide

Clinical uses

- Effective in treating essential hypertension & hypertension in patients with :

  - High plasma renin activity (young & white people)

- Ischemic heart disease.

- Diabetic nephropathy .

- Treatment of heart failure .

Adverse effects

- Severe hypotension
- Acute renal failure in patients with renal artery stenosis.
- Hyperkalemia
- Dry cough,wheezing ,angioedema
- Captopril may cause neutropenia (**decrease in WBC**) , proteinuria (**protein in urea**) & loss of taste.

Contraindications:

- During the second and third trimesters of pregnancy due to the risk of : fetal hypotension ,anuria ,renal failure & malformations .
- Bilateral renal artery stenosis or stenosis of a renal artery with solitary **(** كليه واحده دون الأخرى**)** kidney.

Drug interactions:

- With potassium-sparing diuretics
- NSAIDs impair their hypotensive effects by blocking bradykinin-mediated vasodilatation.

Team Note:

ACEI Characteristics

Unlike vasodilators ; no reflex sympathetic activation;

so they can be used safely in patients with ischemic heart disease.

Drugs	Mechanism	Use	Adverse effect
Captopril, enalapril and ramipril	Inhibition the synthesis of angiotensin II. The stimulation of Kallikrein-Kinin system.	Effective in treating essential hypertension & hypertension in patients with : - High plasma renin activity (young & white people) - Ischemic heart disease. - Diabetic nephropathy . Treatment of heart failure .	Severe hypotension Acute renal failure in patients with renal artery stenosis. Hyperkalemia Dry cough,wheezing ,angioedema Captopril may cause neutropenia (decrease in WBC) , proteinuria (protein in urea) & loss of taste .

Angiotensin receptor –blocking drugs:

- Mechanism of action :

  Block AT_1 receptors. (AT_1 → angiotensin 1)

- Advantages over ACEI :

1- They have no effect on bradykinin system causing neither: cough,wheezing nor angioedema

2- Complete inhibition of angiotensin 11actions.

Losartan

- Orally effective
- Has a potent active metabolite.
- Long half-life, taken once daily.
- Can not cross BBB

Adverse effects:

- As ACEI except for cough ,wheezing , and angioedema. .(**alrgic adema**)
- Same contraindications as ACEI.

هنا مقارنه طلبت مني دكتوره عزه اعملها ..

Comparison between ACEI & Angiotensin Rs blocker

	Mechanism	Adverse effect
ACEI (Captopril, enalapril and ramipril **)**	- Inhibition the synthesis of angiotensin II. - The stimulation of Kallikrein-Kinin system. (activte the bradykanin)	- Severe hypotension - Acute renal failure in patients with renal artery stenosis. - Hyperkalemia - Dry cough,wheezing ,angioedema Captopril : may cause neutropenia (decrease in WBC) , proteinuria (protein in urea) & loss of taste .
Angiotensin receptor –blocking drugs (Losartan)	Block AT_1 receptors. Advantages over ACEI : 1- They have no effect on bradykinin system causing neither: cough,wheezing nor angioedema 2- Complete inhibition of angiotensin 11actions.	As ACEI except for cough ,wheezing , and angioedema (alergic adema). Same contraindications as ACEI.