

### Complications of high blood pressure

Blood

:pressure can lead to the following

1. MI (Myocardial Infarction)
2. CVA (Cerebro Vascular Accident)
3. Kidney failure
4. Intracranial hemorrhage
5. Bleeding from the eyes

Blood pressure regulation consists of 4 pillars: heart rate, environmental resistance, venous capacity and blood volume

The sympathetic system affects 3 of these 4 pillars: heart rate, peripheral resistance, and venous capacity. The fourth pillar is mostly a function of kidney function, which affects both peripheral vascular resistance and blood volume by secreting renin and producing angiotensin II and aldosterone.

### Blood pressure regulating sites

:Locations for regulating blood pressure are

- 1 Heart
- 2 Arteries
- 3 Kidney
4. Vasomotor center in brainstem
- 5 Baroreceptor reflex .

### Calculation and types of blood pressure

) Blood pressure (BP) (derived from cardiac output (CO) (in peripheral vascular resistance) (PVR) )

$$BP = CO * PVR$$

:Blood pressure can be divided into two types

Primary or Essential (and secondary).

More than 52% of cases are %

primary and less than 12% of cases are secondary.

There are various causes for secondary blood pressure, including % Cardiovascular disorders, Cushing's disease and drug-induced

### Principles of blood pressure treatment

💡 , If the blood pressure is **mild** it can be relieved with lifestyle modification and non-drug treatment. The following should be considered in lifestyle modification

1. Weight loss, this case alone can be mmHg 22 -5 .Reduce blood pressure
2. ( Dietary controls 8 -14 mmHg (and reducing food sodium intake) 2 -8 mmHg)
3. ) mmHg 5-4 ( Sport
4. ( Reduce alcohol consumption 2 -4 mmHg )

💡 If high blood pressure is **not treated** , antihypertensive drugs are used. The choice of drug is based on the patient's concomitant diseases and risk factors. Medication is started at a low dose and gradually increased. If .not treated with the first drug, the second drug is added

💡 :Among the causes of **failure of** blood pressure treatment, the following can be mentioned

1. The patient does not have good compliance and does not follow the medication regimen
2. Drug interactions and interfering diseases that have caused high blood pressure

3. .Secondary hypertension has occurred

### Different classes of antihypertensive drugs

1. Diuretic
2. :Sympatoplegics (sympathetic inhibitors) (including

- a Sympathetic central blockers alpha 2 (agonists)
- b Ganglionic inhibitors .
- c. Sympathetic nerve terminal blockers
- d. Alpha and beta receptor blockers (beta blocker and alpha blocker)
- 3. Ca<sup>2+</sup> Channel Blocker (CCB) vasodilator and calcium channel blocker ( Or calcium antagonist)
- 4. :Renin-angiotensin system inhibitors include
  - a. Angiotensin converting enzyme (ACEI ) inhibitor
  - b Angiotensin .ARB receptor antagonist( II )
  - c Renin . inhibitors

#### ) First-line treatment drugs FIRST LINE AGENT (

1. Thiazide diuretic
2. Calcium channel blocker
3. Angiotensin converting enzyme inhibitor
4. Angiotensin receptor antagonist

### Reminder of diuretics

Mechanism: Thiazide diuretics inhibit Na-Cl cotransporter by acting on the initial part of the distal tubule .

Thiazide diuretics and potassium preservatives are important in this class .of drugs

○ Thiazide diuretics include: **hydrochlorothiazide, chlorthalidone and metolazone** . These drugs can be used alone or in combination with other drugs. Concomitant use of these diuretics with drugs affecting renin .angiotensin or beta-blockers may have a synergistic effect

#### Application

1. Treatment of hypertension
2. Isolated Systolic Hypertension( ISH )
3. Heart failure (with drugs such as ACEI (

#### Complications and effects

1. Impotence
2. Increased renin
3. Increased concentrations of calcium, glucose, uric acid and cholesterol
4. Decreased concentrations of sodium, potassium and magnesium

#### Drug Interactions

Triamterene and losartan cause hyperkalemia, which is modulated in combination with hydrochlorothiazide H<sub>2</sub>O, which has a hypokalemic effect

.They increase lithium and digoxin poisoning

**Hydrochlorothiazide:** Available in 25 and 50 mg tablets. It is available in combination with triamterene and losartan H<sub>2</sub>O.

**Available in** 25, 50 and 120 mg tablets. It is mostly used in hospitals to treat high blood pressure, edema and

- The most important potassium-sparing diuretics are **spironolactone and eplerenone**

**Spironolactone:** is an aldosterone antagonist and is used in treating patients with heart failure

**Eplerenone:** This drug is also an aldosterone antagonist but has no anti-androgenic effects of spironolactone. Like spironolactone, it causes hyperkalemia

It is also used to treat heart failure after MI. Due to the concentration of serum creatine, in more than 2 mg / dl in men and more than 1.5 mg / dl in women, it is contraindicated

**Mechanism:** Potassium-sparing diuretics inhibit the action of aldosterone by acting on the main cells of the distal distal regions and cortical collecting ducts. Spironolactone and Amiloride block the action of aldosterone, and trimethoprim and amiloride cause hyperkalemia by disrupting the functions of sodium channels

**Metolazone** is used in heart failure and is effective in

Master Book: Diuretics have 2 effects

first effect is due to a decrease in blood volume with a decrease in cardiac output, but after several weeks of their use, cardiac output returns to normal, but blood pressure remains at a moderate level, because in this case the second effect is diuretic. Means a decrease in environmental resistance that modulates blood pressure

2 Decreased environmental resistance is due to reduced intracellular calcium. This is due to the reduction of sodium in the body and the effect on the mechanism of sodium-calcium exchange that causes an increase in intracellular calcium concentration, which eventually causes vasodilation.) Amiloride directly reduces intracellular calcium

However, the antihypertensive effect of diuretics is weak and blood pressure is reduced to 15-12 mmHg is obtained

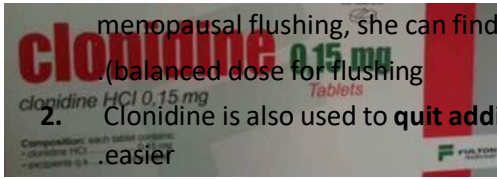
## Sympatoplegic (anti-adrenergic blood pressure or sympathetic inhibitor) 1 Central . sympathetic blockers or alpha<sub>2</sub> agonists (affecting the CNS (reducing sympathetic tone ,

, Drugs in this category include **clonidine and methyl dopa**. They reduce both cardiac output and vascular resistance easily entering the CNS. They have a compensatory response in the form of water and salt retention.

**Clonidine** has 25 and 100 mg tablets. The dose is between 1 and 6 tablets per day. Even if not taken for a long time, it can cause some side effects such as constipation, depression and bradycardia. Sudden cessation can lead to a rebound crisis.

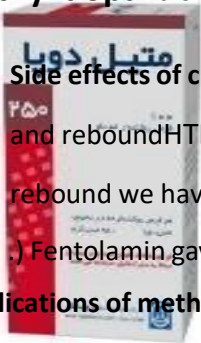
.Clonidine is not widely used today to discuss high blood pressure. It is one of the last categories, but it has features

1. For example, it can relieve **menopausal flushing in women** . If a woman has high blood pressure and menopausal flushing, she can find a place (even if she does not have high blood pressure, she is prescribed a (balanced dose for flushing
2. Clonidine is also used to **quit addiction** because it alleviates withdrawal symptoms and makes quitting a little easier
3. . for **migraines** , but it is the drug of choice for beta-blockers



.**Methyl dopa** It is used for blood pressure in pregnancy because it does not have adverse effects on the fetus

**Side effects of clonidine** : Postural hypotension, drowsiness, dry mouth and rebound HTN With a sudden cessation of that hypertensive ( rebound we have to either give the drug again or an alpha blocker like .) Fentolamin gave



.**Complications of methyl dopa** : positive Coombs test, sometimes even hemolytic anemia, severe drowsiness

**Sympathetic inhibitors** are among the most potent antihypertensive drugs. These drugs depend on the ganglia or filaments

Peripheral sympathetic nerves are affected, they have different effects. Drugs affecting the sympathetic ,centers (the most important of which are clonidine and methyl dopa) (such as depression, nightmares sleep disorders, nightmares and orthostatic hypotension), while **drugs affecting the ganglia** , in addition ,to paralysis Sympathetic and parasympathetic paralysis also have side effects such as constipation .urinary retention, dry mouth and impaired vision

## Outside margin of the booklet

**2. Sympathetic ganglion inhibitors** are among the most popular drugs in

.this class, including tri-meth

**Mechanism:** These drugs inhibit the nicotinic receptors of the presynaptic and parasympathetic nerves of the .sympathetic and peripheral nerves

.Two important drugs in this group are reserpine and guanethidine

.Mechanism: Reserpine depletes norepinephrine and inhibits the release of norepinephrine

.Side effects of reserpine include depression and guanethidine, orthostatic hypotension, and sexual dysfunction

And like ganglion blockers, due to severe autonomic complications such as orthostatic .hypertension, they are rarely used in the treatment of hypertension and are obsolete

## 4 Alpha and beta sympathetic receptor blockers (adrenergic receptors) .

### 1 beta blockers)

Beta-blockers reduce cardiac output and heart rate. They also reduce renin concentrations by blocking the 1B receptor on adjacent glomerular cells . These drugs also .have central effects

The first reduces blood pressure by reducing cardiac output and the second by inhibiting RAAS

They reduce vascular resistance. These drugs also have effects

on the CNS , but are not among the first-line drugs (the first line was thiazide

1. In a patient who, in addition to high blood pressure, also has a migraine headache. Beta-blockers are one of the best drugs to prevent migraine headaches (in younger people, they will respond better

2. In patients with ischemic heart disease or angina pectoris, beta-blockers have the effects of controlling ischemic heart disease
3. In patients after myocardial infarction, re-stroke is prevented
4. Beta blockers control tremor and tachycardia-
5. In patients with hyperthyroidism, they reduce the symptoms of anxiety, palpitations and tremors
6. ACEI and diuretics in people older than 62 . years

### Special effects of 3 types of beta-blockers

- 1 .Cardioselective **atenolol** , **metoprolol** Selective beta blocker ( 1 % ) That focus on the heart
- 0 Outside the booklet, maybe the master forgot to say it is important! Non-selective ( . beta-blockers reduce cardiac output and after a few days reduce renin, resulting in . peripheral vascular resistance, such as **propranolol** and **nadolol**
- 3 In addition to the beta receptor, they also block alpha, thus having vasodilator effects: **labetalol** , **carvedilol** .  
lip , ♦ □ ● ✕ □ □ ☹ ● □ ● , **Nabivolol** , **carvedilol** , **carovone**

We do not know why the professor said here, but the books are considered a separate category from .adrenergic receptor blockers

### Complications

1. Decreased exercise tolerance, as a result, causes fatigue
2. Impotence, due to decreased cardiac output
3. , Some, such as **propranolol** , worsen the condition of heart failure patients, and some, such as **carvedilol** .improve the condition of heart failure
4. Exacerbates Vessel spasm ( Raynaud s disease (meaning peripheral vascular disease)'PVD ) .
5. .They aggravate and prolong hypoglycemia
6. .They have metabolic effects on lipids and blood sugar
7. Some of them also aggravate asthma

### Starting dose

- ✓ : **Propranolol** 82 mg : **Metoprolol** 52 mg : **Atenolol** mg 25
- ✓ : **Carvedilol** mg 6525 2 times a day up to a maximum dose of 25 mg , 2 times a day
- ✓ : **Bisoprolol** mg 5 -255 Dedicated 1 % )

**Propranolol** **Propranolol**: Inhibitor of  $\beta_1$  and  $\beta_2$  receptors , which weakens the force of contraction and reduces heart rate. Out of the booklet: It has the most ) complication of bronchospasm and asthma prohibition and we give metoprolol instead

**Carvedilol** **Coreg ( Carvedilol** (: must ) With food Consume to reduce the rate of .absorption and prevent hypotension

**Metoprolol** **Metoprolol** **Available** in both tartrate and succinate. Succinate for the : ) preparation of a slow release product Sustained release And previous failure is ( .used Metoprolol selectively affects the  $\beta_{receptor}$  It is preferred to non-selective . drugs (such as propranolol) for asthma, diabetes, and PVD .

**Bisoprolol** **Bisoprolol** : Available as 5-12 mg tablets . It is used in blood pressure and heart failure. In heart failure with a dose of 15 25 mg. Started and gradually increased according to the patient's tolerance

### 2) (Alpha blocker) Alpha antagonist

**1. Antagonists** Drugs such as **prazosin, doxazosin, terazosin** are in this category. They reduce vascular : contractions by inhibiting vascular alpha receptors. These drugs have no place in the discussion of blood pressure today. They have beneficial effects on blood lipids. These drugs are used for both BPH and to treat high blood pressure, but it is noteworthy that the alpha blocker used for BPH .is specific to prostate receptors

. Cited urinary incontinence and ( postural hypotension ) agonists: hypotension □ 1 Complications

, Overall, the use of prazosin and terazosin is very low. While being careful Because they are alpha-blockers these drugs give a reflex heartbeat. A reflex heartbeat reduces some of the effects of the drug itself. Because they dilate blood vessels, they become swollen or swollen over time. Edema also reduces some of the effects of the drug. So if we want prazosin to have a good effect, we must combine it with a diuretic and a beta-

blocker. Diuretic for bloating and beta-blocker for heartbeat. Well, it is usually less used with such a pattern and has no place in the four groups.

2. Agonists ! We can mention clonidine and methyl dopa, which were explained separately :

### 3 ) Vasodilator and calcium channel blocker .CA<sup>2+</sup> CHANNEL BLOCKER ( CCB Or calcium ( antagonist

#### Vasodilators\_

These drugs dilate blood vessels by acting directly on smooth muscle through a non-atomic mechanism. These are useful in high blood pressure

Vasodilators are divided into 4 categories based on : the mechanism of action

**NO releases** : hydralazine, nitroprusside and nitroglycerin  
**Potassium channel openers**  
 Minoxidil and diazoxide  
**Calcium channel blockers**  
**(CCBs)** Amlodipine :

**Receptor agonist** (Phenoldopam) Phenoldopam - is a short acting injectable and long-acting and is used in emergency blood pressure

#### Minoxidil

It has pills for blood pressure and lotions and shampoos for hair loss. This drug opens potassium channels and causes hyperpolarization and relaxation of cells in smooth muscles. It has a greater effect on the vein and is used in severe HTN.

#### :Complications

Vasodilators reflex tachycardia in the heart) Wherever

.blood vessels dilate in response Heart rate rises

Prolonged use of minoxidil may cause edema, as it reduces renal blood circulation and releases renin, resulting in aldosterone, which retains water and salt

Hirsutism, facial hair growth, pericardial effusion, and angina exacerbation

. Minoxidil is not the drug of choice but is used in resistant patients who have not responded to previous drugs

#### Diazoxide

The mechanism is to open the potassium channel. This drug is in the form of ampoules and is one of the HT emergency drugs. But unlike nitroprusside, it has a long effect

🍷 In the form of slow IV . It enters the body and **lowers the pressure**

🍷 This drug, like octreotide, inhibits the release of insulin from pancreatic beta cells, and this feature of the drug is taken orally in a condition called **Use insulinoma**<sup>1</sup> Which is the picture of diabetes - This drug should not be injected into a person who has had a stroke because it gives reflex tachycardia and complicates the heart condition

: **Complications** HTN , drop hyperglycemia, water and salt retention, sodium retention

#### SODIUM NITROPRUSSIDE \_ \_

<sup>1</sup> Insulin secretory tumor



**Mechanism:** It causes dilation by releasing NO in smooth muscle cells

This drug dilates the arteries and veins and is the best **emergency medicine** for **high blood pressure**

Sodium nitroprusside is marketed in the form of ampoules and consumed in the form of infusion. And is added to Baxter (serum)

Next to the ampoules of this medicine, there is an aluminum foil to cover the serum set with foil when using the medicine, because this medicine is very sensitive to light and heat

### Complications



1 In the chemical formula of this drug, there is cyanide, which if used in high doses can release cyanide in the body, causing cyanide poisoning. Hydroxycobalamin is used to relieve cyanide poisoning. It absorbs cyanide and converts it to cyanocobalamin (a vitamin)<sub>12</sub> B .converts)

**Booklet margin :** On the other hand, if taken in therapeutic doses, the liver adds cyanide, sulfur, and CN<sup>-</sup> to SCN<sup>-</sup> (thiosulfate), from which thiosulfate is excreted from the body

**Symptoms of cyanide poisoning** include: bitter almond odor, changes in seizures and coma ,

Continued side effects (outside the booklet)  
2 Severe pressure drop  
3 Tachycardia )  
4 Hyperuricemia )  
5 Hyperglycemia )

Similar to nitroprusside, the NO release mechanism in the endothelial cell dilates the artery and most of the arterioles

It is available in the form of pills and ampoules and is one of the safest drugs during pregnancy. Of course, this drug is less used today

### Complications

1. Lupus-like syndrome, which is dose-dependent and below 222 .mg per day, is not common

Headache	.2
Tachycardia	.3
Angina pectoris	.4
Severe fluid retention	.5

## 2 ) (Calcium channel blocker) $Ca^{2+}$ CHANNEL BLOCKER (CCB Or calcium antagonist (

reduces both impulse transmission in the conduction system of the heart and heart rate

, Reduce. The most important drugs in this category are **amlodipine** , **nifedipine**

**Verapamil** and **diltiazem** can be named CCBs : are divided into two types CCB drugs lower blood pressure using the following two mechanisms:

1 **Dihydropyridines** , such as nifedipine and amlodipine ) 1 **Inhibition of voltage-dependent calcium** channels (type .L channels) in muscle

2 **Non-dihydropyridine** , such as diltiazem and Verapamil ) is smooth and heart-healthy, which reduces the

### Different effects of two types of CCB :

heart rate and its contractile force, as well as  
.reducing cardiac output

2. **(Inhibition of vascular calcium channels** that cause vasodilation

1 Dihydropyridines have many effects on vasodilation. While on ) the environmental resistance of PVR .

SA and AV .nodes have little effect

2 Non-dihydropyridines have significant effects on the heart and less on the arteries. Therefore, drugs such as )

.verapamil are expected to have good effects in treating arrhythmias

When prescribing CCB for a patient with heart failure, we  
.choose a drug that has vascular effects and no heart effects  
Dihydropyridines

**Amlodipine** is widely used

Its Indian brand name is Amlodipine. The half-life of this drug is high ( 35-50 hours ) , so it is taken once . a day

### Clinical application of CCB :

Both types of CCB .can be used to treat high blood pressure and ischemia

Verapamil is stronger than diltiazem in every way. Increases the force of heart contraction, has an effect on  
AV and SA nodes and vasodilation .

Arrhythmia treatment

Treatment of achalasia (lower esophageal sphincter  
(stenosis

Topical application of diltiazem ointment in relieving

stroke sphincter contraction

Diphtheria leads to preterm labor by relaxing the  
.smooth muscle

In conditions such as peripheral vascular disease PVD  
and cases where only systolic blood pressure is high  
or (Isolated  
systolic hypertension (ISH) dihydropyridines are ,  
.preferable to non-dihydropyridines

### CCB : complications

1 Headache )

2 ) Flushing or flushing

3 .High doses of these may cause ankle edema )

4 especially with verapamil<sup>2</sup> Constipation )

5 If these drugs, especially non-dihydropyridines, are used in high doses, they can cause **severe bradycardia and )**  
**. heart block**

The limiting factor in the administration of amlodipine and nifedipine is **reflex tachycardia** . It should be noted that  
.diltiazem and verapamil cause bradycardia

## 4 Renin-angiotensin system inhibitors .

. It is widely used in the discussion of blood pressure, ischemia of the heart and heart failure

### ACE INHIBITORS .1



These drugs are known as "prils", such as **captopril** , **enalapril** , **lisinopril** , **benzapril** and  
**.fusinopril** , which are the first three drugs available in Iran

These drugs inhibit angiotensin converting enzyme inhibitors and prevent the conversion of  
angiotensinI toII .

### ARB .2



These drugs are known as the sartan family and are angiotensin II receptor antagonists(II Receptor Blocker ,such as **losartan** , **losartan** , candesartan , (ibersartan , **telmisartan** , and  
.saralazine. This family is in Iran

### Mechanism of action of ACEI and ARB :

Angiotensinogen produced by the liver is influenced by renin to angiotensinI. Becomes. Renin also by **Aliskiren** is  
.inhibited

Angiotensin I is converted to angiotensinII bykininase II ( ACE ). ACEI .drugs work with lunch of this enzyme

ACE also inactivates bradykinin (a vasodilator), soACEIs reduce angiotensinII production which is a vasoconstrictor ,  
(and prevent bradykinin inactivation), which is a dilator. Is vascular (cause Severe vasodilation resulting in  
.hypotension

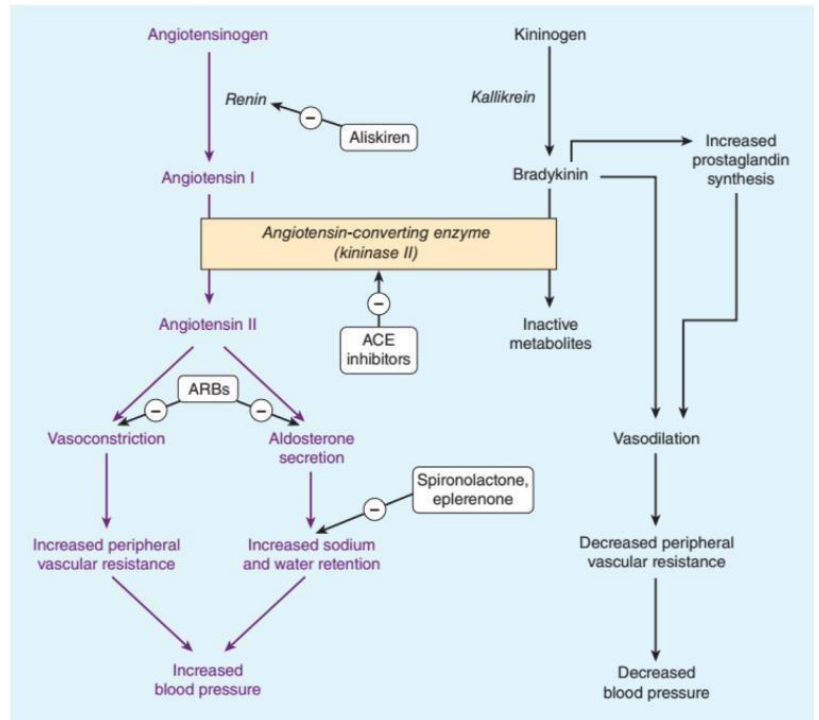
AngiotensinII .by acting on its receptor, causes blood vessels to constrict and secrete aldosterone ,

ARB drugs Like losartan, they block angiotensinII .blocking their effects and lowering blood pressure ,<sup>3</sup> receptors

Drugs such as spiro lactone and applerone, which are aldosterone antagonists, block the effects of  
.aldosterone and lower blood pressure

<sup>2</sup> Due to the effect on the calcium channels of smooth muscle

<sup>3</sup> The name of this receptor isAT1



#### Side effects of ACEI and ARB :

- 1 Mild hyperkalemia And mild (can even be severe) )
- 2 ) Severe hypotension in the first dose of the drug )<sup>st</sup> dose hypotension 1 so these drugs are started with low ,( doses and gradually increase the dose according to the patient's tolerance until the desired result
- 3 )ACEIs cause cough dryin 5-32% of cases Due to increased levels of bradykinin and substanceP in the .body
- 4 )ACEIs suppress bone marrow in some people and Pancytopenia. Creates
- 5 )ACEIs <sup>4</sup> They can also cause \_angioneurotic edema.
- 6 Impaired sense of taste with captopril )
- 7 Concomitant use of these two classes of drugs with thiazides ) .can have a synergistic effect and reduce blood pressure too much

#### ContraindicationsACEI andARB :

- 1 In pregnancy, especially in the second and third trimesters )
- Renovascular Diseases ) 2
- 3 Bilateral renal artery )stenosis because angiotensin ,II affects efferentarteriol more thanAfferent arteriol By . blocking the function of angiotensinGFR , II is reduced andazotemia .occurs

<sup>4</sup> ,Because of these side effectsARB is often preferred toACEI .

## :applications

1 <sup>5</sup>.**Diabetes** : Medications prevent diabetic nephropathy )

2 **Heart failure** : The renin-angiotensin system is very active in heart failure, so using this drug to suppress the )  
.high activity of this system is effective

3 **Chronic kidney disease )(CKD)**

4 **Proteinuria** : Angiotensin )II causes the efferent artery to constrict, so proteinuria is reduced by taking these drugs  
.and dilating the efferent arteries

Treatment of cysteine stones: Captopril, like penicillamine, has a thiol group that )  
.causes the excretion of cysteine 5  
After Remodeling: Improves MI and improvesEF . )  
6

## :Drug interactions

.These two groups, along with spironolactone, eplerenone, and potassium salts, can cause dangerous hyperkalemia  
NSAIDs such as ibuprofen and indomethacin reduce the effectiveness of these drugs  
.Both classes of drugs increase the risk of lithium poisoning by increasing blood lithium concentrations

**GroupRI ) Renin Inhibitor (Aliskiren** The newest antihypertensive drug that is a renin inhibitor. Its side effects :  
.include headache and diarrhea (in high doses) but does not cause cough  
can cause cough and angioedema but it will be less severe than ,ACEI Other complications of .ACEI .are not  
known The important thing about this drug is that it is metabolized by CYP 3A4 .and can cause extensive drug

## 3 Renin inhibitors .

<sup>5</sup> Even if the patient is Normotensive .these drugs are used to prevent renal nephropathy

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