ANGIOTENSIN-CONVERTING ENZYME INHIBITORS

Angiotensin converting enzyme (ACE) inhibitors are highly popular drugs in the treatment of hypertension.

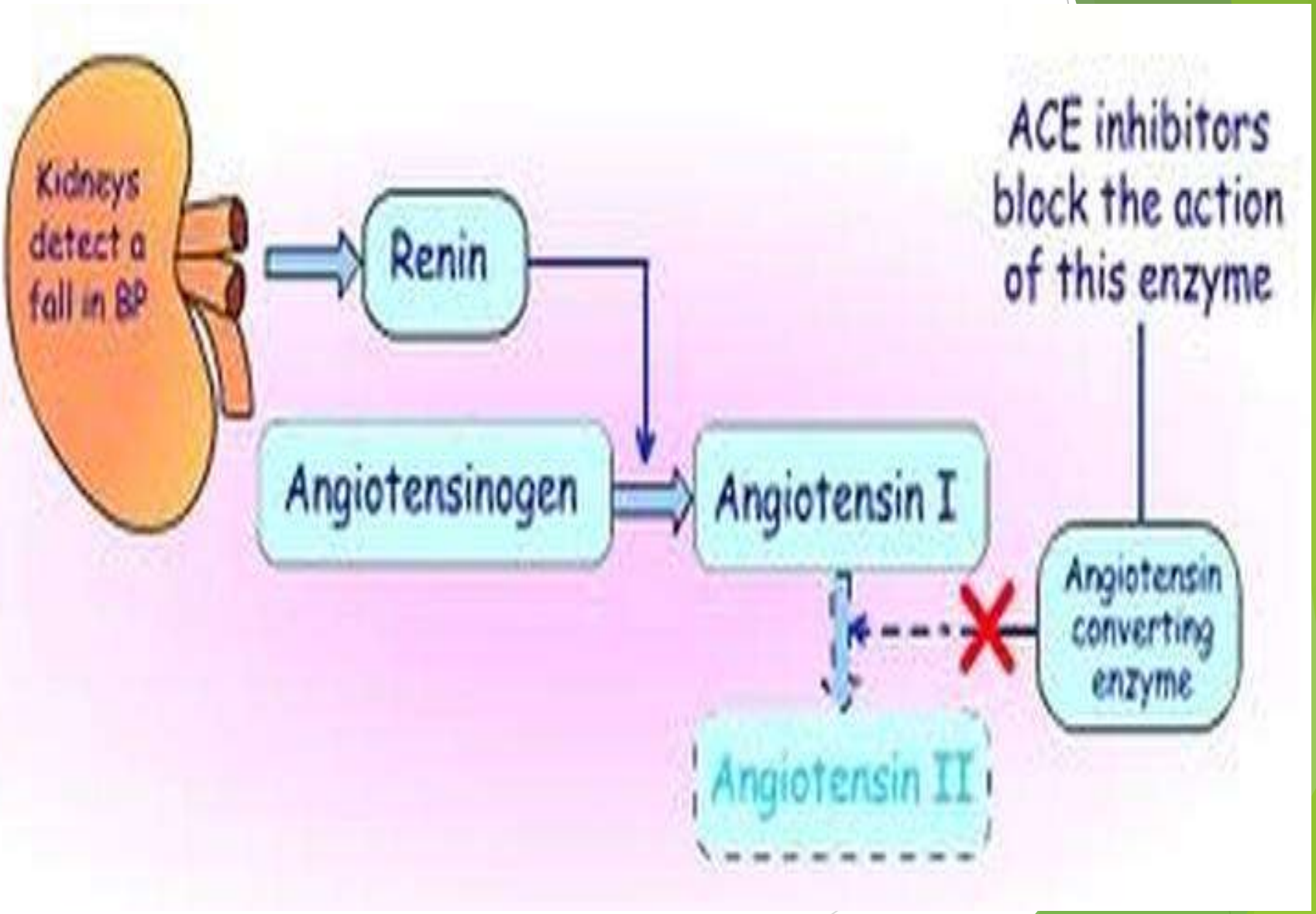
Examples include benazepril, captopril, enalapril, fosinopril, lisinopril, quinapril, & ramipril.

In general, these drugs are well absorbed from the GI tract, reaching peak serum conc. within 1 to 4 hours.

Enalapril & ramipril are prodrugs & require hepatic metabolism to produce their active forms These drugs are primarily eliminated through the kidneys.

ACEIs binds directly to the active site of

ACE, which is found in the lung and vascular endothelium, preventing the conversion of angiotension I to angiotensin II. Because angiotensin II is a potent vasoconstrictor and stimulant of aldosterone secretion, so prescription of ACEIs cause: vasodilation; decreased peripheral vascular resistance; decreased blood pressure; increased cardiac output; and a relative increase in renal, cerebral, and coronary blood flow.


Kidneys detect a fall in BP
Renin
Angiotensinogen
Angiotensin I
Angiotensin II
Angiotensin converting enzyme
ACE inhibitors block the action of this enzyme

The hypotensive response may be severe in select patients after their initial dose, resulting in syncope and cardiac ischemia.

Patients who are hypovolemic from concomitant diuretic use appear to be at greatest risk.

However, these drugs are well tolerated and have a very low incidence of side effects.

Some reported adverse effects include rash, hyperkalemia, chronic cough, and angioedema.

ACEIs are teratogens and should never be used by pregnant women.

ACEI-Induced Angioedema

Angioedema is an inflammatory reaction in which there is increased capillary blood flow & permeability, resulting in an increase in interstitial fluid.

If this process is confined to the superficial dermis, urticaria develops; if the deeper layers of the dermis or subcutaneous tissue are involved, angioedema results.

Angioedema most commonly involves the perioral, or oropharyngeal tissues. This swelling may progress rapidly over minutes & result in complete airway obstruction & death.

The pathogenesis of angioedema involves multiple vasoactive substances, including histamine, prostaglandin D2 , leukotrienes, & bradykinin.

ACE inhibition results in elevations in bradykinin concentrations that appear to be the primary cause of both ACE inhibitors-induced angioedema & cough.

The overall incidence of ACE inhibitors-induced angioedema is only approximately 0.1%, & it is idiopathic.

Treatment varies depending on the severity and rapidity of the swelling. Because its involve the tongue, face, and oropharynx, treatment involves maintenance of airway (with nasopharyngeal airway, intubation, or surgical intervention, depending on the case).

All patients with mild or quickly resolving angioedema should be observed for several hours to ensure that the swelling does not progress or return.

Outpatient therapy with a short course of oral antihistamines and corticosteroids is appropriate. Such patients should be instructed to discontinue ACEI therapy permanently and to consult their primary care physicians about other antihypertensive options. Because this is a mechanistic and not allergic adverse effect, the use of any other ACEIs is contraindicated]

Angiotensin-converting enzyme inhibitor overdose:

- Although several reports of overdoses involving ACE inhibitors have been published, the majority of the cases reported manifested toxicity of a coingestant. Hypotension may occur in select patients, but deaths are rarely reported in isolated ACE inhibitors ingestions. Other patients may remain asymptomatic despite high serum drug concentrations.

Treatment should focus on supportive care & on identifying any coingestants that may be more toxic, particularly other antihypertensives such as β-blockers or calcium channel blocker

In most cases, AC alone is sufficient GI decontamination. IV crystalloid boluses are often effective in correcting hypotension, although in rare cases, catecholamines may be required.

Naloxone may also be effective in reversing the hypotensive effects of ACE inhibitors (ACE inhibitors may also inhibit the metabolism of enkephalins and potentiate their opioid effect which includes lowering of blood pressure).