Angiotensin II Receptor Blockers (ARBs)

Angiotensin II receptor blockers (ARBs) are a class of drugs that work by blocking the action of angiotensin II. They do this by preventing angiotensin II from binding to angiotensin II receptors on the smooth muscles that blood vessels. This results in the dilation of blood vessels and reduction in blood pressure.

Angiotensin II Receptor blockers are among the many classes of antihypertensives. In this article, we shall cover more about this class of drugs. If you missed our previous article on diuretics and angiotensin-converting enzyme inhibitor you can access them here.

- Diuretics
- Angiotensin-converting enzyme inhibitor

Target cells have a type of receptors known as AT1 and AT2 receptors.

Most of the physiological actions of angiotensin are mediated via the AT1 receptor.

Transducer mechanisms of AT1 inhibitors:

In different tissues show different mechanisms. For example PhospholipaseC-IP3/DAG-intracellular Ca++ release mechanism vascular and visceral smooth muscle contraction.

In myocardium and vascular smooth muscles AT1 receptor mediates long term effects by MAP (Mitogen-activated protein kinase and others.

Mitogen-activated protein kinases are serine or threonine-specific protein kinases which respond to extracellular stimuli such as osmotic stress, and proinflammatory cytokines. This MAP regulates various cellular activities, such as gene expression, mitosis, differentiation, proliferation, and cell survival/apoptosis(programmed cell death).

Examples of Angiotensin Receptor Blockers

Losartan and **valsartan** were the first and most common drugs of the angiotensin II type 1 (AT1) receptor.

Others are;

1. **Candesartan,**
2. **eprosartan,**
3. **irbesartan,**
4. **telmisartan,** and
5. **olmesartan.**

Losartan is the specific AT1 blocker. A competitive antagonist and inverse agonist of the AT1

receptor. It does not interfere with other receptors except TXA2.

This drug blocks all the actions of Angiotensin II which are; vasoconstriction, sympathetic stimulation, aldosterone release and renal actions of salt and water reabsorption with no inhibition of angiotensin-converting enzyme.

Theoretically, Losartan is more superior over ACEIs:
With its use, cough is rare.

It does not induce any interference with bradykinin and other ACE substrates and is, therefore, more selective angiotensin blockers than ACE inhibitors.

Its use is associated with complete inhibition of AT1 – alternative remains with ACEs.
Result in indirect activation of AT2 – vasodilatation which is an additional benefit.

Ideally, the clinical benefit of ARBs over ACEIs is not known.

However, losartan produces a decrease in blood pressure in hypertensive patients which is for a long period (about 24 Hrs), heart rate remains unchanged and cardiovascular reflexes are not interfered with.
There is no significant effect in plasma lipid profile, insulin sensitivity and carbohydrate tolerance, etc but there may be a mild uricosuric effect.

Pharmacokinetic:

Absorption of Losartan is not affected by food but unlike ACEIs its bioavailability is low.

It has a high first-pass metabolism.
Losartan is carboxylated to active metabolite E3174.
It is highly bound to plasma protein.
Lastly, it does not enter the brain.

What are the side effects of ARBs?

ARBs are well tolerated by most people. The most common side effects are

- cough,
- elevated potassium levels in the blood (hyperkalemia),
- low blood pressure,
- dizziness,
- headache,
- drowsiness,
- diarrhea,
- abnormal taste sensation (metallic or salty taste),
- rash,
- orthostatic hypotension (low blood pressure upon standing),
- fatigue,
- indigestion,
- increased blood glucose levels,

- flu-like symptoms,
- sinusitis (sinus infection),
- bronchitis, and
- upper respiratory tract infections.

Compared to Angiotensin-converting enzyme inhibitors, cough occurs less often with Angiotensin Receptor Blockers.

Serious side effects of ARBs

- Fatal, but rare, side effects are
    - kidney failure,
    - liver failure (hepatitis),
    - serious allergic reactions,
    - A decrease in white blood cells,
    - A decrease in blood platelets, and
    - Foetopathic like Angiotensin-converting enzyme inhibitors
    - Rare 1st dose-effect hypotension
    - Lower incidence of angioedema

Losartan is available as 25 and 50 mg tablets.

Are ARBs safe to take if I'm pregnant or breastfeeding?

ARBs are not prescribed for women during pregnancy because they may cause oligohydramnios.