ANGIOTENSIN RECEPTOR ANTAGONISTS / ANGIOTENSIN RECEPTOR BLOCKERS

Losartan, candesartan, valsartan and irbesartan (sartans) are non-peptide, orally active AT_1 receptor antagonists (ARBs). ARBs differ pharmacologically from ACEIs, but behave similarly to ACEIs apart from **not causing cough** and angioedema (do not increase bradykinin), reducing cardiovascular morbidity and mortality (including stroke) compared with placebo in hypertension. ACE is not the only enzyme capable of forming angiotensin II, chymase (which is not inhibited by ACEIs) provide another alternative route. It is not known if alternative pathways of angiotensin II formation are important in vivo, but if so, then *ARBs could be more effective than ACEIs when such alternative pathways are active*. Again, it is not known whether any of the beneficial effects of ACEIs are bradykinin/NO mediated. It is therefore unwise to assume that ARBs will necessarily share all the therapeutic properties of ACEIs, although there is considerable overlap in the clinical indications for these drugs.

Losartan (this phenyl tetrazole substituted imidazole compound acts as a selective, competitive blocker of angiotensin II receptor type 1 (AT_1) and decreases peripheral vascular resistance) results in the production of active metabolites in the liver. Losartan is also a competitive antagonist of TXA_2 and attenuates platelet aggregation. All indications, adverse effects (i.e. can cause fetotoxicity, neuropsychiatric disturbances such as insomnia, confusion, nightmares, agitation and depression) and contraindications of ACEI also apply to ARB except that incidence of cough and angioedema is less with ARB.

Valsartan, Irbesartan, Eprosartan, Telmisartan, Candesartan, Olmesartan and Azilsartan are the other analogues of losartan. Therapeutically ACEI and ARB are equally effective for treatment of hypertension. The choice between them depends upon familiarity and cost. Whether ARBs offer the same degree of cardioprotection as ACEI is not known. ARB have similar contraindications as ACEI.

RENIN INHIBITORS

Aliskiren, Remikiren and Enalkiren are the drugs that inhibit the enzyme renin. So these drugs will decrease the activity of RAAS causing fall in blood pressure. These drugs can be used orally for the treatment of chronic hypertension.

Aliskiren, an orally active non-peptide renin inhibitor, was developed and registered as an antihypertensive drug. It causes dose-dependent, direct inhibition of the plasma renin activity and thereby reduces both angiotensin I and II levels, and produces fall in BP, but has adverse effects that include diarrhoea (common), acute renal failure, cardiovascular events in patients with diabetes mellitus, and, rarely, angioedema and severe allergic reaction.

Class	Drug[a]	Pharmacokinetics	Adverse effects[b]	Uses	Notes
ARBs	Valsartan	$t_{1/2}$ ~6 h	Hypotension Reversible renal impairment (in patients with renal artery stenosis)	Hypertension Heart failure	ARBs are cleared by hepatic metabolism
	Losartan	Long-acting metabolite $t_{1/2}$ ~8 h	As valsartan	As valsartan Diabetic nephropathy	Irbesartan is similar, with $t_{1/2}$ ~10–15 h
	Candesartan	$t_{1/2}$ 5–10 h Long-acting because receptor complex is stable	As valsartan	As valsartan	Given as prodrug ester (candesartan cilexetil)
Renin inhibitor	Aliskiren	Low oral bioavailability $t_{1/2}$ 24 h	As valsartan, also diarrhoea	Essential hypertension	The FDA has warned against combining with ACEI or ARB in patients with renal impairment + diabetes mellitus

Renin angiotensin aldosterone system and target of drugs