

The background features a dark blue gradient with a subtle pattern of white circular lines and arrows, some of which are part of a larger scale or gauge. The scale has numerical markings from 140 to 260 in increments of 10. The text is centered in a bold, white, sans-serif font.

ANGIOTENSIN II RECEPTOR BLOCKERS: MORE THAN THE ALTERNATIVE

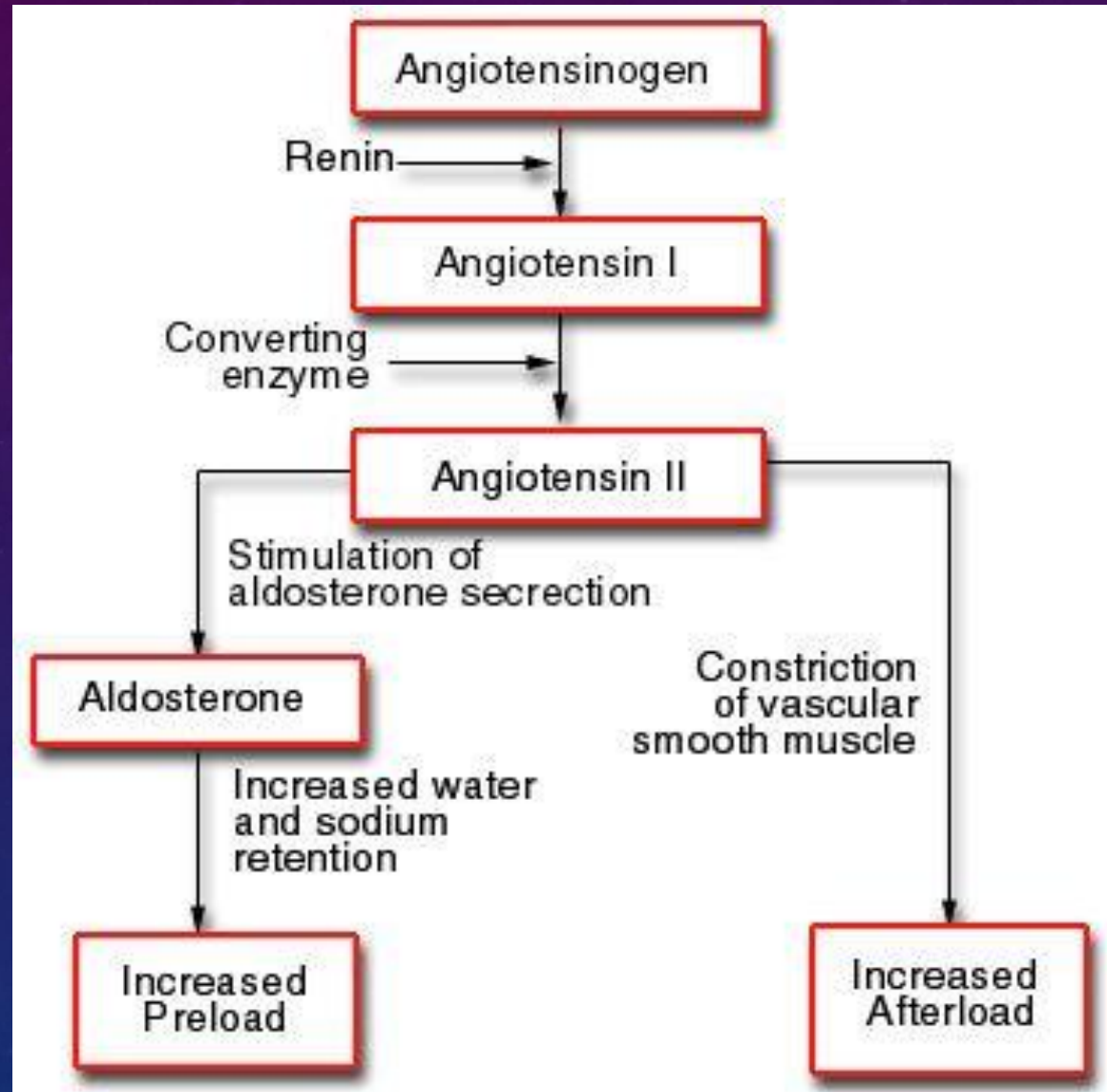
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RENIN-ANGIOTENSIN ALDOSTERONE SYSTEM (RAAS) INHIBITORS

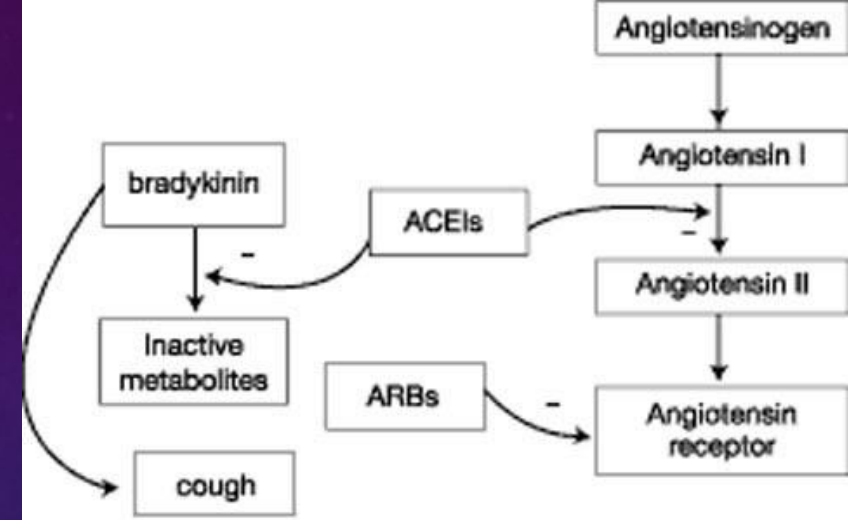
- Indicated for hypertension, congestive heart failure, diabetic nephropathy
- Physiologic Effects:
 - Dilate arteries and veins, thereby reducing arterial pressure
 - Promote renal excretion of sodium and water by blocking the effects of angiotensin II in the kidney and on aldosterone secretion
 - Inhibit cardiac and vascular remodeling associated with chronic hypertension, heart failure, and myocardial infarction

RAAS INHIBITORS: MECHANISM OF ACTION

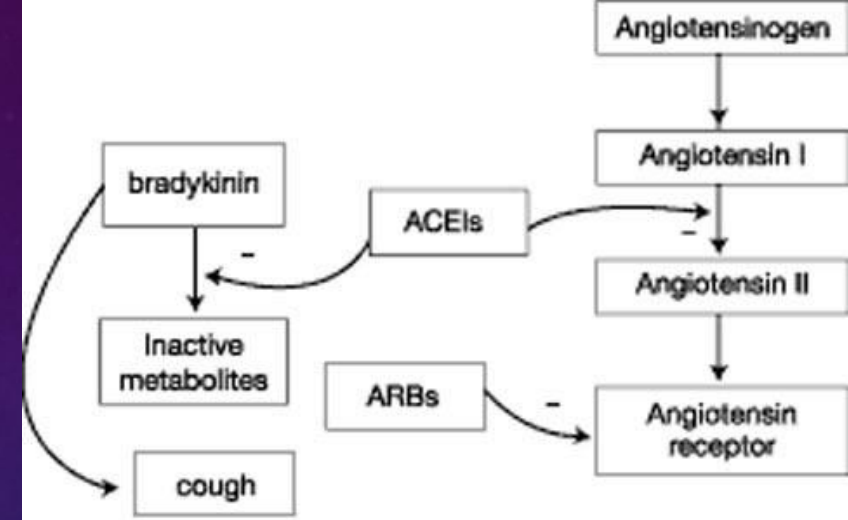


THE PROBLEM WITH ACE INHIBITORS

- Between 5% and 20% of patients treated with ACE inhibitors experience a dry persistent cough that requires termination of therapy
- “ACE cough” results from the concurrent blockade of bradykinin breakdown
 - A dry, hacking cough that can be incapacitating
 - Bradykinin accumulates, causing bronchoconstriction
 - Angioedema can also result from bradykinin buildup
- Higher incidence of cough & angioedema in certain populations
 - ACE cough is more common in women
 - African-Americans had a relative risk of 2.68 for ACE cough & higher risk for angioedema
 - 46-47% of Chinese had a relative risk of 2.58 of discontinuing ACE inhibitors due to cough
- Where both are indicated, ACE inhibitors are typically used first, followed by Angiotensin II Receptor Blockers (ARBs) if intolerance develops



ANGIOTENSIN II RECEPTOR BLOCKERS



- Works to lower blood pressure using the same pathway as ACE inhibitors
- ARBs do not inhibit the breakdown of bradykinin or other kinins, thus reducing the risk for persistent dry cough and/or angioedema
 - Double-blind trial randomized hypertensive patients who experienced ACE cough (whose cough disappeared on placebo) to losartan 50 mg, lisinopril 20 mg, hydrochlorothiazide (HCTZ) 25 mg, or placebo for 8 weeks found that incidence of cough using losartan therapy is similar to that associated with placebo therapy
- Well tolerated with a safety profile similar to placebo: dizziness, hypotension, diarrhea
- ARBs are non-inferior, or just as effective, as ACE inhibitors

NON-INFERIORITY TRIALS – ARE ARBS JUST AS GOOD AS ACE INHIBITORS?

- Non-inferiority trials demonstrate that the efficacy of one drug (ARBs) is not significantly inferior to that of another therapy (ACEs)
- Two areas
 - Cardioprotection
 - Renoprotection

NON-INFERIORITY TRIAL – ONTARGET

- Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial
- Compared the ACE inhibitor ramipril 10 mg daily, the ARB telmisartan 80 mg daily, and the combination of the two drugs in patients with vascular disease or high-risk diabetes with end-organ damage
- 8576 assigned to ramipril, 8542 assigned to telmisartan, and 8502 assigned to receive both drugs; excluded those with hypotension, elevated creatinine
- Outcome: Death from CV causes, myocardial infarction, stroke, or hospitalization for heart failure
- Conclusion: Telmisartan was equivalent to ramipril in patients with vascular disease or high-risk diabetes and was associated with less cough and angioedema.

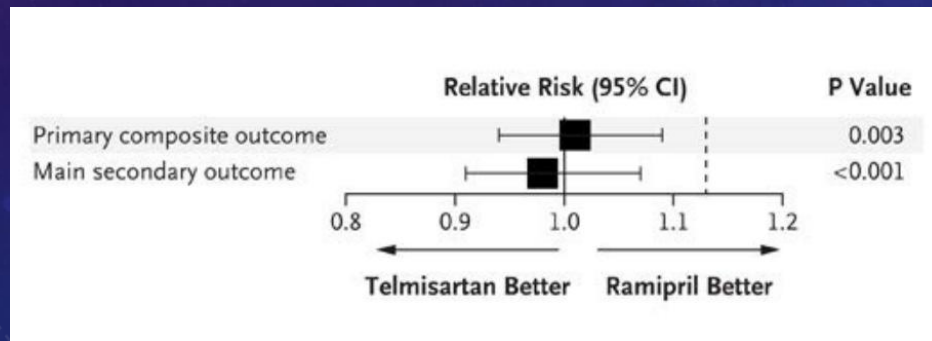


Table 2. Discontinuation of Study Medications and Selected Reasons for Permanent Discontinuation.*

Variable	Ramipril (N=8576)	Telmisartan (N=8542)	Combination Therapy (N=8502)	Telmisartan vs. Ramipril		Combination Therapy vs. Ramipril	
				Relative Risk	P Value	Relative Risk	P Value
Total no. of discontinuations†	2099 (24.5)	1962 (23.0)	2495 (29.3)	0.94	0.02	1.20	<0.001
Reason for permanent discontinuation							
Hypotensive symptoms	149 (1.7)	229 (2.7)	406 (4.8)	1.54	<0.001	2.75	<0.001
Syncope	15 (0.2)	19 (0.2)	29 (0.3)	1.27	0.49	1.95	0.03
Cough	360 (4.2)	93 (1.1)	392 (4.6)	0.26	<0.001	1.10	0.19
Diarrhea	12 (0.1)	19 (0.2)	39 (0.5)	1.59	0.20	3.28	<0.001
Angioedema	25 (0.3)	10 (0.1)	18 (0.2)	0.4	0.01	0.73	0.30
Renal impairment	60 (0.7)	68 (0.8)	94 (1.1)	1.14	0.46	1.58	<0.001

NON-INFERIORITY TRIAL – VALIANT

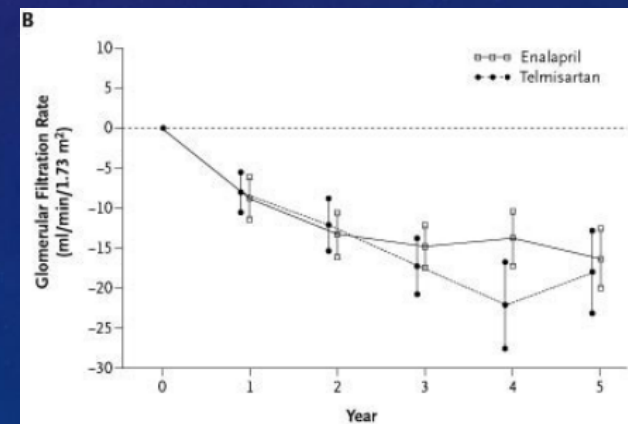
- VALsartan In Acute myocardial iNfarctIon - Prospective, multinational, double-blind, randomized, active-control study; 14,703 patients from 24 countries
- Compared ACE inhibitor captopril 50 mg TID, the ARB valsartan 160 mg BID, and the combination of the two drugs (valsartan 80 BID + captopril 50 mg) in patients with heart failure and/or left ventricular systolic dysfunction after acute myocardial infarction
- Patients with hypotension, creatinine > 2.5 mg/dL, or prior intolerance to either an ACE inhibitor or ARB were excluded from the study

	Valsartan	Captopril	Valsartan + Captopril	
All-cause mortality (n%)	979 (19.9)	958 (19.5)	941 (19.3)	
Endpoint	No. of endpoints (%)		Valsartan vs Captopril	
	Valsartan	Captopril	Hazard ratio (97.5% CI)	P Value for Noninferiority
CV death	870 (16.8)	830 (16.9)	0.98 (0.87-1.09)	.001

	Valsartan	Captopril	Valsartan + Captopril
Hypotension	1.4*	0.8	1.9*
Renal causes	1.1	0.8	1.3*
Hyperkalemia	0.1	0.1	0.2
Cough	0.6*	2.5	2.1
Rash	0.3*	0.8	0.7
Taste disturbance	0.2*	0.4	0.3
Angioedema	0.2	0.3	0.2
Any of the above events	4.0*	5.7	6.8
Any adverse event	5.8*	7.7	9.0
Any reason	20.5	21.6	23.4*

NON-INFERIORITY – TYPE 2 DIABETES & NEPHROPATHY

- Prospective, multicenter, double-blind, five-year study with 250 subjects with type 2 diabetes and early nephropathy were randomly assigned to receive either the angiotensin II–receptor blocker telmisartan (80 mg daily, in 120 subjects) or the ACE inhibitor enalapril (20 mg daily, in 130 subjects).
- The primary end point was the change in the glomerular filtration rate between the baseline value and the last available value during the five-year treatment period.
- Conclusion: Telmisartan is not inferior to enalapril in providing long-term renoprotection in persons with type 2 diabetes. These findings support the clinical equivalence of angiotensin II–receptor blockers and ACE inhibitors in persons with conditions that place them at high risk for cardiovascular events.



SUMMARY

- Where indicated, ACE inhibitors and ARBs share the same role in therapy, yet ACEs is typically used first despite being characterized by cough and angioedema.
- ARBs avoid the problem of “ACE cough” and angioedema, and are well tolerated with a safety profile similar to placebo.
- ARBs are reserved as the alternative if intolerance develops.
- When it comes to vascular and renal protection, ARBs are just as good as ACE inhibitors and without the problems they carry.

The background is a gradient from dark purple at the top to dark blue at the bottom, overlaid with a field of small white stars. On the right side, there are several technical diagrams: a large circular scale with numerical markings from 80 to 210, a smaller circular diagram with concentric lines and arrows, and a dashed circular path with an arrow. On the left side, there are faint circular outlines and arrows.

Questions?