Managing Hypertension Using Combination Therapy

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Related letter: Race-Based Treatment Decisions Perpetuate Structural Racism (https://www.aafp.org/afp/2020/0801/p136.html)

Patient information: A handout on this topic is available at https://familydoctor.org/high-blood-pressure-medicines (https://familydoctor.org/high-blood-pressure-medicines).

Related *FPM* article: Coding for Hypertension: Painting a Picture of the Severity of Illness (https://www.aafp.org/fpm/2020/0300/p23.html)

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More than 70% of adults treated for primary hypertension will eventually require at least two antihypertensive agents, either initially as combination therapy or as add-on therapy if monotherapy and lifestyle modifications do not achieve adequate blood pressure control. Four main classes of medications are used in combination therapy for the treatment of hypertension: thiazide diuretics, calcium channel blockers, angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin receptor blockers (ARBs). ACEIs and ARBs should not be used simultaneously. In black patients, at least one agent should be a thiazide diuretic or a calcium channel blocker. Patients with heart failure with reduced ejection fraction should be treated initially with a beta blocker and an ACEI or ARB (or an angiotensin receptor–neprilysin inhibitor), followed by add-on therapy with a mineralocorticoid receptor antagonist and a diuretic based on volume status. Treatment for patients with chronic kidney disease and proteinuria should include an ACEI or ARB plus a thiazide diuretic or a calcium channel blocker. Patients with diabetes mellitus should be treated similarly to those without diabetes unless proteinuria is present, in which case combination therapy should include an ACEI or ARB.

Cardiovascular disease is the leading cause of death worldwide, and hypertension is a modifiable risk factor for cardiovascular disease.[1] Risk increases with incremental increases in blood pressure, even within the normal range.[2] More than 70% of adults treated for primary hypertension will eventually require at least two antihypertensive agents.[3]

WHAT'S NEW ON THIS TOPIC

Hypertension Therapy

A meta-analysis showed that angiotensin-converting enzyme inhibitors—but not angiotensin receptor blockers—reduced the incidence of doubling of the serum creatinine level in patients with diabetes mellitus, but it did not affect progression to end-stage renal disease. Another meta-analysis showed that angiotensin-converting enzyme inhibitors were superior to angiotensin receptor blockers for reducing all-cause and cardiovascular mortality.

Compared with monotherapy, initial combination therapy achieves blood pressure control more quickly with similar tolerability. However, in a randomized controlled trial, patients who started on monotherapy eventually achieved blood pressure control similar to that of patients who started on combination therapy.

Although improved adherence to antihypertensive medications is expected to decrease morbidity and mortality, a large systematic review found that the effects of fixed-dose combination therapy on all-cause mortality or atherosclerotic cardiovascular disease events are uncertain.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

CLINICAL RECOMMENDATION	*EVIDENCE RATING*	*COMMENT*
For most patients, combination antihypertensive therapy should include an ACEI or ARB, a thiazide diuretic, or a calcium channel blocker.[4–6]	**A**	Consistent evidence showing reduced morbidity and mortality with each of those four drug classes in RCTs included in guidelines

CLINICAL RECOMMENDATION	EVIDENCE RATING	COMMENT
Patients with chronic kidney disease who have proteinuria should be prescribed an ACEI or ARB as part of combination therapy.[40,41]	**A**	Consistent evidence from RCTs showing reduced morbidity and mortality
The combination of an ACEI and an ARB should be avoided.[43]	**B**	RCT showed that benefit is outweighed by increased morbidity

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; RCT = randomized controlled trial.

A = consistent, good-quality patient-oriented evidence; **B** = inconsistent or limited-quality patient-oriented evidence; **C** = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afpsort (https://www.aafp.org/afpsort).

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