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 EVMS  
 Journal Club

**P-In patients who present to the ED with asymptomatic HTN**

**I- Is the use of one specific class of anti-hypertensive agent**

**C- compared to routine use of a variety of agents**

**O- associated with consistent, safe, and patient focused (ie expensive/side effects) results**

Question:

In a patient with asymptomatic HTN presenting to the ED is one class of anti-hypertensive medications more efficacious than any other class of anti-hypertensive medication?

Clinical Scenario:

A 55 year old black diabetic patient presents to the ED for a refill on her metformin. Vitals are BP 162/110 HR 90 SpO<sub>2</sub>% 98% RA. The patient has no complaints and is unaware of any previous diagnosis of HTN.

Search Strategies:

PubMed was searched using the words “treatment for asymptomatic hypertension” AND English [language] AND Humans [terms]. 1580 articles resulted from search of those 22 articles were reviewed 9 relevant articles were identified.

Author, date and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Cochrane review First line drug for HTN 2009	24 trials with 28 arms which include 58, 040 patients	metanalysis	Thiazides reduced mortality (RR 0.89), stroke (RR 0.63), CHD (RR 0.84) and CVS (RR 0.70). Beta-blockers reduced stroke (RR 0.83) and CVS (RR 0.89) but not CHD (RR 0.90) or mortality (RR 0.96). ACE inhibitors reduced mortality (RR 0.83), stroke (RR 0.65), CHD (RR 0.81) and CVS (RR 0.76). CCB's reduced stroke (RR 0.58) and CVS (RR 0.71) but not CHD (RR 0.77) or	First-line low-dose thiazides reduce all morbidity and mortality outcomes	metanalysis

<p>Cochrane review Beta-blockers for HTN 2009</p>	<p>13 RCT's (N 91, 561) comparing beta-blockers to placebo, CCB's, Renin angiotensin system inhibitors, and diuretics</p>	<p>metanalysis</p>	<p>All cause mortality worse for BB than CCB's (RR 1.07). BB on CVD was worse than CCB's (RR 1.18) but no different compared to RAS or diuretics.</p>	<p>Beta Blockers should not be used as first line anit-HTN</p>	<p>Multiple different beta-blockers used. Metanalysis. No differentiation for age</p>
<p>ONTARGET NEJM 2008</p>	<p>25, 620 high risk patients with cardiovascular disease or diabetes randomized to ramipril, telmistartin, or combination</p>	<p>Double blinded prospective RCT</p>	<p>Primary outcome was seen 16.5% ramipril, 16.7% telmisartan, and 16.3% combined. Telmisartan had less cough and angioedema</p>	<p>Telmisartan was equivalent to ramipril in pt with vascular disease or high risk DM and was associated with less angioedema. Combination no benefit and more adverse outcomes</p>	<p>(1) 60% were already on an ACE inhibitor, weeding out those who were intolerant; (2) those who were known to be intolerant to an ACE inhibitor were shunted to a parallel study, Telmisartan Randomized Assessment Study in ACE Intolerant Subjects With Cardiovascular Disease, which has not yet been published; and (3) ramipril was given for a 3- to 4-week run-in so that, again, those who were quickly intolerant of an ACE inhibitor were not enrolled.</p>
<p>ACCOMPLISH NEJM 2008</p>	<p>11, 506 pt with HTN who were at high risk for cardiovascular event were randomized to benazpril plus HCTZ or amlodipine</p>	<p>Double blinded prospective RCT</p>	<p>Primary outcome was seen in the 9.6% of the benazpril-amlodipine group vs 11.8% in the benazpril-HCTZ group (relative risk reduction</p>	<p>Blood pressure reductions were similar in both groups but the benazpril-amlodipine group had significantly less cardiovascular</p>	<p>This cohort represents a high risk population over a third of the pt in each group had coronary revascularization. 60% of the pt had DM, of which HCTZ probably is not</p>

			19.6%)	events in high risk patients	optimal htn treatment. Used 25mg of HCTZ.
ASCOT Lancet 2005	19,342 pt 40-79 yo with $\geq 3$ CAD risk factors were randomized to amlodipine 5mg (plus perindopril as needed) or atenolol 50mg (plus bendroflumethiazide as needed)	Double blinded prospective RCT	Stopped after median of 5.5 years. Amlodipine group had fewer MI (8.2 vs 9.1 per 1000), strokes (6.2 vs 8.1 per 1000), and CV events and procedures (27.4 vs 32.8 per 1000) lower mortality (13.9 vs 15.5 per 1000) and developing DM (11 vs 15.9 per 1000)	Lower rates of CV disease and mortality in amlodipine vs atenolol in pt with no active CV disease	95% white, 77% male, 63% older than 60. 2.7 mmHg difference in SBP between the two groups possible contributing to the difference in CV events
Outcomes in hypertensive black and nonblack patients treated with chlorthalidone, amlodipine, and lisinopril  JAMA 2005	Subgroup analysis from the ALLHAT study	Retrospective subgroup analysis	No significant difference between treatment groups for the primary CHD outcomes. Clorithalidone had lower rate of HF than amlodipine (RR 1.37). in lisinopril group chlorthalidone had less risk of stroke or CVD (RR 1.4 and 1.19)	Thiazide diuretics remain the drug of choice for initial drug therapy	Retrospective subgroup analysis
ANBP2	6083 patients with	Open label	Both groups	ACEi had	Open label. 95%

NEJM 2003	HTN aged 65-84 yo were randomized to an ACEi or Diuretic	prospective RCT	decreased BP by 26/12 mmHg, CV events favored ACEi (56.1 vs 59.8 per 1000) [HR 0.89]	better outcomes than diuretics particularly in elderly men	white.
INVEST JAMA 2003	22, 556 patients with HTN and known CAD were randomized to verapamil or atenolol (with trandolapril and/or HCTZ added as needed)	Open label prospective RCT	Similar BP control. No difference in primary outcomes or secondary outcomes	Verapamil was as clinically effective as atenolol	Open label. Used JNC 6 guidelines.
ALLHAT JAMA 2002	33, 357 patients with htn aged 55 years or older with one CHD risk factor randomized to chlorthalidone, amlodipine, or lisinopril	Double blind prospective RCT	At nearly 5 year f/u similar reduction in BP, the incidence of Primary outcomes and all cause mortality was the same. Amlodipine has higher rates of HF than chlorthalidone (10.2% vs 7.7%). Lisinopril had higher rates of CV dz (33.3 vs 30.9%), stroke (6.3 vs 5.6%), and HF (8.7 vs 7.7%) than chlorthalidone	Thiazide diuretics are superior in preventing 1 or more forms of CVD and are less expensive	The most common used thiazide in the US is HCTZ. Question whether the lisinopril arm is handicapped secondary to inappropriate add on therapy., use in blacks.

**Clinical Bottom Line:**

It appears much more important to lower the blood pressure in order to achieve the blood pressure requirements found in the JNC-7 than it does what anti-hypertensive medication to start first line. Thiazide diuretics have proven to be as efficacious as newer medication and significantly cheaper making them a good first line anti-hypertensive medication.

Beta-blockers stand out as the only anti-hypertensive medication as a class that should be avoided as first line agent. Given this thiazide diuretics with special attention given to chlorthalidone should be started as first line anti-hypertensive medication for patients who it is decided should be treated for their hypertension from the emergency department.

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