

Pills for Mild (Stage 1) Hypertension

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Hypertension Risks

Each increment of 20 mm Hg in systolic blood pressure or 10 mm Hg in diastolic blood pressure doubles the risk of cardiovascular disease across the entire blood pressure range from 115 / 75 to 185 / 115 mm Hg.

Hypertension Trends

- Between 1960 and 1991, BP decreased 10 mm Hg systolic and 5 mm Hg diastolic on average in USA
- Hypertension in 18 – 74 year olds declined from 36.3% from 1960 – 1962 to 20.4% from 1988 – 1991
- Deaths from stroke and cardiovascular disease have declined by 60% and 53%, respectively.
- Changes in lifestyle are responsible for most of the reduction in complications of hypertension
 - Less saturated fat
 - Fewer smokers
- This favorable trend is reversing with obesity epidemic: in 2000, 4% more with hypertension than in 1991

Hypertension Stats

- HBP most common reason to see a doctor in the U.S.: 35 million office visits per year
- HBP diagnosis and treatment
 - 70% are aware of their diagnosis,
 - 59% are on treatment
 - 34% are controlled (blood pressure less than 140 / 90 mm Hg)

Recommended Lifestyle Modifications*

- Weight reduction
- DASH eating plan**
- Dietary sodium reduction
- Physical activity increase
- Regular aerobic physical activity
- Moderation in drinking alcohol

*The National High Blood Pressure Education Program

**Dietary Approaches to Stop Hypertension

Drug Categories

- Thiazide Diuretics (TDs)
- Beta-blockers (BBs)
- Calcium Channel Blockers (CCNs)
- ACE Inhibitors (ACEIs)
- Angiotensin II Receptor Blocker (ARBs)
- Alpha Blockers (ABs)
- Others

Mild Hypertension

- The evidence-basis for drug treatment of mild hypertension (stage 1) consists of 14 placebo-controlled trials that included stage 2 patients mixed in with stage 1 patients.

Thiazide Diuretics (TDs)

- Reduce the mean blood pressure by about 14 mm Hg for those taking an average American diet and 9 mm Hg for those taking a low sodium diet
- Trials with stages 1 and 2 HBP: 3/5 showed clinical benefit
- Trials with stage 2 HBP: 8/10 showed benefit
- Oslo Trial: healthy men, ages 40-49, stages 1-2
 - Endpoint: Death from coronary artery disease 10 yrs
 - Hydrochlorothiazide: 14, Placebo: 3, $P < 0.01$).

Risks of TDs

- Increase serum cholesterol
- Increase blood glucose
- Reducing blood potassium
- Increase blood viscosity

Beta-Blockers (BBs)

- Placebo-controlled RCTs only for atenolol and propranolol
- 1/6 RCTs showed benefit (42% fewer strokes in stage 2 patients 60-79 years old)
- BBs only “second-line” therapy (JNC-6)
- Risks
 - Decreased sexual ability
 - Drowsiness
 - Insomnia
 - Tiredness
 - Weakness

Calcium Channel Blockers (CCBs)

- 5 RCTs of CCBs versus placebos
 - Clinical outcomes confounded by concurrent use of thiazides
 - No RCTs of stage 1 HBP patients
- Meta-analysis comparing HBP drugs: CCBs the worst
- Risks
 - Flushing
 - Headache
 - Edema
 - Dizziness
 - Fatigue
 - Nausea
 - Palpitations
 - Acute toxicity
 - 56 deaths / year
 - 244 serious adverse reactions / year

ACE Inhibitors (ACEIs)

- 4 RCTs with ACEIs versus placebos
 - 2 showed no clinical benefit in any endpoint
 - 1 had fewer strokes when combined with thiazides
 - 1 had slower progression to kidney Dz in DM patients
 - No RCTs with stage 1 patients
- Risks
 - Diarrhea
 - Dizziness
 - Fainting
 - Fatigue
 - Cough

Angiotensin II Receptor Blocker (ARBs)

- 4 RCTs: Reduce proteinuria in renal disease (surrogate endpoint) in all and cardiovascular endpoints (clinical endpoints) in one.
- Side effects: less than other HBP drugs
 - Dizziness
 - Abdominal pain
 - Anxiety
 - Chest pain
 - Diarrhea
 - Indigestion
 - Fatigue
 - Headache

Alpha Blockers (ABs)

- No placebo-controlled HBP RCTs
 - Doxazosin (Cardura) and Hytrin (terazosin) FDA approved to improve difficulty with urination associated with BPH.
 - Prazosin (Minipress) pills no longer marketed

Risks

- Dizziness
- Drowsiness
- Fatigue
- Headache

Other BP Meds

- Clonidine (Catapres)
- Methyldopa
- Reserpine
- Labetalol
- Hydralazine (Apresoline)
- Minoxidil (Lonitin)
- Carvedilol (Coreg):

RCTs: none for any of them

ALLHAT

- Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial
- TDs, BBs, CCBs, ACEIs, ABs
- No placebo arm
- Endpoints
 - Death
 - myocardial infarction
 - stroke
- TDs superior to all others for at least one clinical endpoint
- Doxazosin (Cardura) did harm

Evidence for Benefit of Drugs for Stage 1 HBP

- No RCT evidence of stage 1 patients alone
- Cochrane review pending:
 - Wright JM, Cundiff DK, Gueyffier F.
Antihypertensive drugs for mild hypertension.
(Protocol). *Cochrane Database of Systematic Reviews*. 2007(Issue 3):Art. No.: CD006742.
DOI: 006710.001002/14651858.CD14006742

Evidence for Drug Treatment of Hypertension

- Severe hypertension (systolic blood pressure > 180 mm Hg or diastolic BP > 110 mm Hg): drugs clearly prevent strokes and save lives.
- Moderate hypertension (systolic BP = $160 - 179$ mm Hg and/or diastolic BP = $100 - 109$ mm Hg): benefit less clear.
- Mild hypertension (stage 1 hypertension: systolic blood pressure = $140 - 159$ mm Hg and/or diastolic blood pressure = $90 - 99$ mm Hg): no RCTs show benefit. Drugs may well do harm.

Cost Considerations

- 26 million U.S. residents on HBP meds
- \$22 billion for meds in 2010
- \$14 billion for physician visits in 2010
- Thiazide diuretics least expensive
- 60% of patients with stage 1 HBP
- No evidence for clinical benefit of drug treatment for stage 1 HBP