Pharmacologic Management of Hypertension

Current Concepts In Management of Hypertension

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Secondary Hypertension - Definition
- Renovascular Disease
- (The kidney doesn’t get impressed by blood pressure)
- Renovascular stenosis – Renal artery stenosis
- Fibromuscular hyperplasia
- Atherosclerosis
- Renal Parenchymal Disease
- Polycystic Kidney
- Glomerulonephritis
- Pyelonephritis
- Cushing’s Disease
- Conn’s Syndrome
- Pheochromocytoma
- Catecholamine secreting tumor
- Carcinoid
- Serotonin Secreting Tumor

Secondary Hypertension - Causes
- Renovascular Disease
- (The kidney doesn’t get impressed by blood pressure)
  - Renovascular stenosis – Renal artery stenosis
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  - Atherosclerosis
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- Carcinoid
  - Serotonin Secreting Tumor

Hypertension – Clinical Approach
2. Proper execution of Hypertension Focused Physical Exam
  - Other signs of end organ damage or secondary hypertension
  - Fundi
  - Hypertensive Heart Disease
  - Cerebrovascular Disease
  - Peripheral Vascular Disease
  - Renal, abdominal bruits
  - Femoral pulses
  - Peripheral pulses, edema

Hypertensive Retinopathy - Grade 4

Fundi

Flame fusettes
Hard Exudates
Papilloedema
Cotton Wool Spot
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Hypertension – Clinical Approach

Laboratory Evaluation

- Assess end organ damage
  - ECG
  - Echocardiogram
  - Proteinuria
  - Renal ultrasound
  - Renal function (lytes, BUN, Cr.)

- Screen for treatable causes
  - Renal artery stenosis (fibrinoma, hyper, atheroma)
  - Cushings disease
  - Conn’s Syndrome

- Screen for risk factors (lipids, BS)
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Hypertension – Clinical Approach

When to suspect renovascular hypertension:
- Severe or refractory HT including retinal hemorrhages or papilledema
- Abnormal creatinine may be secondary to bilateral disease
- An acute rise of BP over previous stable baseline
- Proven age of onset before puberty or above 50
- An acute rise of Cr unexplained or after ACE or ARB
- Incidental finding of asymmetric sizes (75% correlation)
- Abdominal bruit that lateralizes (40% sens, 95% spec)
- Negative family history for hypertension

When to suspect other causes of secondary hypertension:
- Primary aldosteronism – hypokalemia and low renin
- Cushings – facies, central obesity, ecchymoses and muscle weakness
- Sleep Apnea – snoring, awake with HA, somnolence
- Coarctation – decreased or lagging peripheral pulses, bruit
- Thyroid abnormalities
- Hyperparathyroidism

Pharmacological Treatment

Compelling indications include a major improvement in outcome independent of blood pressure.

Pharmacological Treatment – Likely to have Favorable Effect

<table>
<thead>
<tr>
<th>Indication</th>
<th>Antihypertensive Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign Prostatic Hypertrophy</td>
<td>Alpha Blocker</td>
</tr>
<tr>
<td>Essential tremor</td>
<td>β-blocker</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>β-blocker</td>
</tr>
<tr>
<td>Migraine</td>
<td>β-blocker, CCB</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Diuretic</td>
</tr>
<tr>
<td>Raynaud’s</td>
<td>Dhp CCB</td>
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</tbody>
</table>

Pharmacological Treatment – Compelling Indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Antihypertensive Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Heart Failure</td>
<td>ACE, ARB, β-blk, hctz, ald-ant</td>
</tr>
<tr>
<td>S/P Myocardial Infarct</td>
<td>ACE, β-blk, ald-ant</td>
</tr>
<tr>
<td>Proteinuric Chronic Renal Insuf</td>
<td>ACE, ARB</td>
</tr>
<tr>
<td>High CAD risk</td>
<td>Diuretic, poss ACE</td>
</tr>
<tr>
<td>Diabetes w/ proteinuria</td>
<td>ACE,</td>
</tr>
<tr>
<td>Diabetes w/o proteinuria</td>
<td>Diuretic, perhaps ACE</td>
</tr>
<tr>
<td>Angina</td>
<td>β-blk, CCB</td>
</tr>
<tr>
<td>Atrial fibrillation / rate control</td>
<td>β-blk, non dhp CCB</td>
</tr>
<tr>
<td>Atrial flutter / rate control</td>
<td>β-blk, non dhp CCB</td>
</tr>
</tbody>
</table>
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### Hypertension – Clinical Approach

#### Pharmacological Treatment – Contraindications

<table>
<thead>
<tr>
<th>Condition</th>
<th>Antihypertensive Drugs</th>
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<tbody>
<tr>
<td>Angio Edema</td>
<td>ACE inhibitor</td>
</tr>
<tr>
<td>Bronchospastic disease</td>
<td>β-blocker</td>
</tr>
<tr>
<td>Depression</td>
<td>Reserpine</td>
</tr>
<tr>
<td>Liver Disease</td>
<td>Methyldopa</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>ACE, ARB</td>
</tr>
<tr>
<td>2nd or 3rd Heart Block</td>
<td>β-blocker, CCB</td>
</tr>
</tbody>
</table>

#### Pharmacological Treatment – Relative Contraindication

<table>
<thead>
<tr>
<th>Condition</th>
<th>Antihypertensive Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>β-blocker, central alpha-agonist</td>
</tr>
<tr>
<td>Gout</td>
<td>Diuretic</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>Aldosterone ant, ACE, ARB</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>Thiazide diuretic</td>
</tr>
<tr>
<td>Renovascular disease</td>
<td>ACE, ARB</td>
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</table>

### Treatment Strategies

#### General Lessons from clinical trials:

- **Efficacy:** Generally, each agent are roughly equally effective - 30 to 50% hypertensive response. However, in a study of 1300: Wide inter-patient variability.
- **Example of enalapril and diltiazem:** No predictable relationship with response from patient to patient.
- **Differential response was most prominent in blacks.**
- **Older black people responded best to diltiazem or hctz.**
- **Younger blacks responded best to diltiazem.**
- **There were fewer differences between the drugs in white patients who responded equally to each of the different drug.** Exception was to HCTZ – Least effective in younger whites.
- **No significant differences in side effects or quality / life**
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**Treatment Strategies**

**General Lessons from clinical trials:**

Does the choice of drug affect the outcome?

The same level of BP control provides the same degree of cardiac protection.

**General Lessons from MCR trials**

Medical Research Council Trial

Found no difference in outcome between thiazide diuretic and propranolol

Atenolol compared to HCTZ/amiloride

Beta blocker reduced the incidence of cerebrovascular disease but doesn’t reduce coronary events or cardiovascular or all-cause mortality.

Diuretic therapy was associated with improvements in all of the end points.

**General Lessons from CAPPP trials**

Captopril Prevention Trial – 10,986 patients

Captopril vs Beta blocker and/or diuretic for six years:

No difference in risk of a cardiovascular event

However in a subsequent sub-group, diabetics had 40% reduction in the relative risk of all primary end points.

**General Lessons from STOP Hypertension 2 and NORDIL study**

6614 elderly/11,00 pts:

Same conclusion. Newer drugs provide similar benefit.

**General Lessons from INSIGHT Trial:**

Same conclusion. Newer drugs provide similar benefit.

No enhanced risk of stroke as in STOP

**Lessons from ALLHAT:**

45,000 Patients with HT + an additional risk factor for CAD.

Clorthalidone vs. lisinopril, amlodipine, doxazosin

Primary outcome: fatal CHD, non-fatal MI. Secondary outcomes: all cause mortality, stroke, combined CVD events

Doxazosin was prematurely terminated because of increased risk of CHF

Efficacy/ control: hair splitting at 2-3 mm Hg over years.

Incidence of primary outcome and all cause mortality were the same.

Higher rate of CHF with amlodipine vs clorthalidone

Lisinopril (vs. clorthalidone) had a higher incidence of combined cardiovascular disease outcomes
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**Treatment Strategies**********

**More Lessons from ALLHAT: subgroups**

Observation observed across all subgroups m,w,b, nb, dm, y.o.

Amlodipine observations consistent with m,w,b, nb, dm, y.o.

Lisinopril observations were consistent with gender, age, dm status, although a few outcome differences among subgroups:

In blacks, increased risk of stroke and combined CVD among blacks with lisinopril over chlorthalidone

Biochemical differences

Hyperkalemia with chlorthalidone

Higher rate of hyperglycemia with chlorthalidone

The adverse metabolic effects did not result in incr CV mortality or morbidity in dm or non dm pt.

**Treatment Strategies**********

**Lessons from VALUE Trial:**

Quickly achieving adequate BP control in high risk patients is very important in groups at high risk.

Variations in cardiovascular outcomes among different antihypertensive drugs and trials can result from relatively small differences in achieved blood pressures.

With equivalent BP control ARBS are at least as effective as CCB’S. Incidence of new onset of diabetes is lower with ARB’s.

THE END