CONCEPT OF DRUG RESISTANT HYPERTENSION

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• Drug resistant hypertension .(1)
  - failure to achieve goal BP.
  - adherence to maximum tolerated doses of 3 antihypertensives of different classes.
  - 3 drugs includes a diuretic.
• Increases risk of fatal and non fatal cardiovascular events:CHF, stroke, MI,CKD

• Linear relationship between BP and CV risk. (1)

• Suboptimal BP control is the most common attributable risk for death worldwide:(2)
  -62% of cardiovascular disease.
  -49% of IHD
  -7.1M deaths/yr.


• Prevalence of RH – unknown.
• Paucity of studies targeted at RH population.
• Achieng Loice, etal, 2008, KNH. (1)
  - good control -26%,
  - with poor BP control, 58% had BP > 160/100 mmHg
• NHANES (2003-2004) 58% had BP < 140/90. (2)
• Cross-sectional analysis of framinghams heart study, only 48% were controlled to < 140/90. (3)
• ALLHAT – Approximately 50% of the participants would have needed ≥ 3 medications for BP control. (4)

1. loice Achieng etal. Adequacy of BP control, level of adherence and reasons for non adherence to antihypertensives at KNH.
Percent of Patients Reaching JNC-7 BP Goals

• Exclude pseudoresistance hypertension.

• Careful evaluation before labelling patient RH
GUIDELINES FOR OFFICE BP ASSESSMENT(1)

- Adequate rest
- Correct cuff sizes
- Right no. of BP readings, adequate intervals.
- Arm support at heart level
- Avoid smoking.

Adherence.

• Loice achieng et al, KNH, 2008. Poor Bp control significantly associated with non adherence.(1)

• of newly dx hypertensive

~40% discontinue their meds during 1\textsuperscript{st} yr.

~40% continue rx over the next decade.(2,3)

• Phase 4 clinical trials, 4783 pts followup 30-330 days. Discontinuation rate~50% in 1 yr.(4)

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White coat effect.(1)

• Clinic BPs persistently elevated
• Out of office BPs normal or lower.
• Check home/ambulatory BPs(2)
• Manifest less TOD, at less CV risk.(3)


OTHER CAUSES OF PSEUDORESISTRANCE

• Heavily calcified/arteriolosclerotic arteries.
• Factors related to meds
  - inadequate dosages
  - inappropriate combinations
  - physicians inertia - REACT STUDY (1)

Factors contributing to RH

- NSAIDS
- Alcohol
- Oral contraceptives/HRT
- Immunosuppressants: steroids, tacrolimus, cs
- Adrenal steroid hormones
- ESAs
- Illicit drugs.
- Liquorice- included in some chewing tobacco.
NSAIDs
- Reduced production of PGI₂
  - Reduced renal blood flow
    - Salt and water retention
    - Sustained BP elevation

Glucocorticoids and mineralocorticoids
- Oxidative stress (reduced NO bioavailability)
  - Vasoconstriction
    - Increased plasma renin concentration
      - RAS activation
      - CNS activation
    - Increased plasma renin activity
      - CNS activation

Cyclosporin
- Oxidative stress (reduced NO bioavailability)
  - Vasoconstriction
    - Increased plasma renin concentration
      - RAS activation
      - CNS activation
    - Increased plasma renin activity
      - CNS activation

Erythropoiesis-stimulating agents
- Reduced hypoxia-mediated vasodilation
  - Increased vascular tone
    - Systemic vasoconstriction
  - Endothelial dysfunction

Illicit substance abuse
- Sustained BP elevation
  - CNS activation
  - Salt and water retention
Factors contributing to RH

• Volume overload
  - Inadequate diuretic therapy
  - excess Na intake.

• Associated conditions
  - obesity
  - non DASH diet
  - DM
  - older age

• Lack of physical exercise.
Other secondary htn causes

- Renal parenchymal disease
- Renal vascular disease
- Primary aldosteronism
- OSA
- Pheomochromocytoma
- Cushings disease
- Thyroid disease
- Aortic coarctation
- Intracranial tumours
Treatment of RH

• PHARMACOLOGICAL

• NON PHARMACOLOGICAL
An Approach to Achieving BP Goal in Resistant Hypertension

Initiate Treatment for Hypertension

(if systolic BP ≥20 mmHg above goal)
START RAS Based Combination therapy
(including thiazide diuretic* or CCB)

Recheck within 3-4 weeks

if BP Still Not at Goal (140/90, general population, 130/80 mm Hg diabetes, CKD)
and agents used are a maximal tolerated dose

Evaluate with Home or 24 hour ambulatory Blood Pressure
and eliminate exogenous substances that raise pressure as well as
secondary causes

Negative
Consider adding vasodilating β blocker** or
Aldosterone Receptor Blocker if obese or
has sleep apnea

Positive
Consider altering timing of medication-
if non-dipper dose at bedtime or after dinner
If adding meds, consider vasodilating β blocker**
Or Aldosterone Receptor Blocker if obese or
has sleep apnea

Recheck within 3-4 weeks
If BP Still Not at Goal

Refer to Clinical Hypertension Specialist

2-drug regimen:

Anti-volume + Anti-RAS

Clinical clues of volume excess (Table 2)
- Option A: optimize diuretic (see Table 3)

Clinical clues of neurogenic HTN (Table 4)
- Option B: treat neurogenic
  - Add (or substitute) β- or α- + β-blockade

Step 2:
- Option A + Option B

Step 3:
- Add spironolactone or CCB (if not yet prescribed)

Step 4:
- Add hydralazine or central α-agonist
How to properly diagnose resistant hypertension

BP >140/90 mmHg in hypertensive patients receiving at least three antihypertensive drugs, including a diuretic, as adequate (full) doses

Check any discrepancies among office, home and 24-h ambulatory BP measurements

Normal home and high clinic and ambulatory BP levels: office-resistant hypertension

Normal home, ambulatory and high clinic BP levels: pseudo-resistant hypertension

All BP above limits

Check patient’s adherence to antihypertensive drug prescriptions

Check patient’s assumption of any interfering drug or substance

Identify and treat possible causes of secondary hypertension and any concomitant condition that may persistently keep BP levels elevated

Optimize and titrate pharmacologic and nonpharmacologic therapies

Refer patient to hypertension center

Source: Expert Rev Cardiovasc Ther © 2010 Expert Reviews Ltd
OTHER TREATMENTS

• ENDOTHELIN RECEPTOR ANTAGONISTS (1)
  - darusentan
• RENAL ARTERY DENERVATION(2,3)
• BRAIN BARORECEPTOR STIMULATION

2. Catheter-Based Renal Sympathetic Denervation for Resistant Hypertension: Durability of Blood Pressure Reduction Out to 24 Months; Symplicity HTN-1 Investigators; Hypertension (Mar 2011)
Renal catheter placement
BRAIN BARORECEPTOR SIMULATION
THE END