New Perspectives in Diagnosis and Treatment of Resistant Hypertension

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Objectives

• Definition and epidemiology of uncontrolled and resistant hypertension
• Discuss diagnostic algorithm of resistant hypertension
• Overview new therapeutic options for resistant hypertension
CASE PRESENTATION

62 years-old female was referred to you for the evaluation and treatment of difficult to control HTN. Her BP is >140/90 in PCP office for several times while taking daily HCTZ 25 mg, Lisinopril 40 mg, and Amlodipine 10 mg. ROS is + for occasional headaches for which she takes “pain killers”. She works as a manager in a local grocery store. On exam, BMI 35 kg/m2, HR 94, BP 164/103. +pitting edema in both ankles. Laboratory findings: glucose 92 mg/dl, K 3.7 mmol/l, Cr 1.0 mg/dL.

What is the next most appropriate step in the management of patient`s hypertension?

1. Add metoprolol 50 mg bid
2. Measure 24-hr urine free cortisol
3. Measure morning aldosterone concentration and plasma renin activity
4. Measure fractionated plasma metanephrines
5. Review medication list including OTC meds, advise to reduce Na intake, encourage 5-7% weight loss and exercise 30 mins/day, encourage to take medications daily
## Classification of Blood Pressure for Adults

<table>
<thead>
<tr>
<th>Blood Pressure Classification</th>
<th>SBP mmHg</th>
<th>DBP mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>and &lt;80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120–139</td>
<td>or 80–89</td>
</tr>
<tr>
<td>Stage 1 Hypertension</td>
<td>140–159</td>
<td>or 90–99</td>
</tr>
<tr>
<td>Stage 2 Hypertension</td>
<td>≥160</td>
<td>or ≥100</td>
</tr>
</tbody>
</table>

*SBP, systolic blood pressure; DBP, diastolic blood pressure*

Definition

• **Uncontrolled hypertension**: blood pressure above goal
  - less than 140/90 for the general population (adults age 18 and older)
  - less than 130/80 in patients with diabetes or CKD

Epidemiology of Uncontrolled HTN

Epidemiology of Uncontrolled Hypertension

Percent of Treated Patients with HTN

- DM: 75%
- CKD: 63%
- Age >75: 60%
- SBP: 90%
- DBP: 48-62%

NHANES 1999-2004, Framingham Heart Study, ALLHAT
Uncontrolled versus Resistant HTN

- **Uncontrolled hypertension**: blood pressure above goal (<140/90, or 130/80 in patients with DM or CKD)
- **Resistant hypertension**:  
  - Office blood pressure that remains above goal (<140/90, or 130/80 in patients with DM or CKD) and  
  - Patient prescribed **3** or more antihypertensive medications **at optimal doses**, including if possible a diuretic  
  or  
  - Office blood pressure at goal but patient requiring 4 or more antihypertensive medications

Why is there a need for definition of resistant hypertension?

“Resistant hypertension is defined in order to identify patients who are at high risk of having reversible causes of hypertension and who may benefit from special diagnostic and therapeutic considerations”.

Epidemiology of Resistant Hypertension

• Largest Data Series from Spain:
  - registry of ~62,000 patients treated for HTN
  - prevalence 12.2% by office BP measurement

• 35% in tertiary care center (Hirsch et al, 2007)
Resistant Hypertension: Diagnosis, Evaluation, and Treatment: A Scientific Statement From the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research
David A. Calhoun, Daniel Jones, Stephen Textor, David C. Goff, Timothy P. Murphy, Robert D. Toto, Anthony White, William C. Cushman, William White, Domenic Sica, Keith Ferdinand, Thomas D. Giles, Bonita Falkner and Robert M. Carey

Approach to Resistant Hypertension

1. Exclude Pseudo-resistance
2. Identify and reverse contributing life-style factors
3. Discontinue or reduce interfering substances
4. Screen for secondary hypertension
5. Pharmacologic treatment
6. Referral to hypertension specialist

Approach to Resistant Hypertension

1. Exclude Pseudo-resistance

2 3 4 5 6
Prevalence of Pseudoresistance

Office BP Measurements
- 12.2% (7.6%)

Ambulatory BP Monitoring
- 62.5%
- 37.5%

Pseudoresistance

- Poor blood pressure measuring technique
- Poor adherence
- White coat effect
Poor BP measuring technique

• Train your staff:
  - Average of 2 readings 1 minute apart after 5 minutes of rest with back supported, use appropriate size of cuff, cuff at the level of R atrium

• Common mistakes:
  - measuring BP w/o letting patient to rest
  - too small cuff

• Less common: acute effect of cigarette smoking, acute effect of coffee, wrist monitor
Poor adherence

• Common!!!
Patterns of persistence with antihypertensive medications in newly diagnosed hypertensive patients

1-yr Adherence to HTN Drug Therapy

- **42%** Discontinuers
- **20%** Continuers
- **22%** Switchers
- **16%** Combiners

42% patients stopped their BP medications within 1st year after the diagnosis of HTN

Rate and determinants of 10-year persistence with antihypertensive drugs.

~40% patients continue to be non-adherent to BP medications

Rate and determinants of 10-year persistence with antihypertensive drugs.

Compliance:
1. Older patients >> younger
2. Men >> Women

Factors leading to poor adherence

- Cost of treatment
- Complexity of treatment
- Side effects
- Instructions not understood
- Organic brain syndrome (e.g. memory deficit)
- Lack of consistent and continuous primary care
White Coat Effect

• Office BP is elevated above goal in the office and significantly higher than at home

• When to suspect:
  - uncontrolled HTN in the office with home symptoms of orthostasis/overmedication

• Diagnosis: Home BP monitoring and ABPM

• Medicare pays for ABPM to exclude white coat hypertension (in untreated patients)
Comparison of office, ambulatory, and self (home) blood pressure monitoring

<table>
<thead>
<tr>
<th></th>
<th>Office BP Monitoring</th>
<th>ABPM</th>
<th>Self-BP Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detects white coat and masked hypertension</td>
<td>No</td>
<td>Yes</td>
<td>Yes (limited)</td>
</tr>
<tr>
<td>Evaluation of therapy</td>
<td>Yes</td>
<td>Yes (limited repeat uses)</td>
<td>Yes</td>
</tr>
<tr>
<td>Normal limit for average risk patients (mm Hg)</td>
<td>&lt; 140/90</td>
<td>&lt;130/80 (24-hour)</td>
<td>&lt;135/85</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;135/85 (awake)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;120/75 (sleep)</td>
<td></td>
</tr>
<tr>
<td>Cost</td>
<td>Low</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Reimbursement</td>
<td>Yes</td>
<td>Partial</td>
<td>No</td>
</tr>
</tbody>
</table>

Approach to Resistant Hypertension

2. Identify and Reverse Contributing Lifestyle Factors
Identify and Reverse Contributing Lifestyle Factors

- Obesity
- Physical inactivity
- Excessive alcohol ingestion
- High salt
- Low fiber diet
## Effect of Weight Loss on BP

<table>
<thead>
<tr>
<th>Weight Loss kg</th>
<th>SBP mm Hg (95&amp;% CI)</th>
<th>DBP mm Hg (95&amp;% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>~ 5.1</td>
<td>-4.44 (-5.93 to -2.95)</td>
<td>-3.57 (-4.88 to -2.25)</td>
</tr>
<tr>
<td>≤ 5</td>
<td>-2.70 (-4.59 to -0.81)</td>
<td>-2.01 (-3.47 to -0.54)</td>
</tr>
<tr>
<td>&gt; 5</td>
<td>-6.63 (-8.43 to -4.82)</td>
<td>-5.12 (-6.48 to -3.75)</td>
</tr>
</tbody>
</table>

Effect of Salt Restriction on Resistant HTN

12 patients with Resistant HTN

1 week of low sodium diet 50meq/day

2-week Washout

1 week of high sodium diet 250meq/day

1 week of low sodium diet 50meq/day

Mean office SBP reduced by 22.7 mm Hg (95% CI of 11.8-33.5) and DBP by 9.1 mm Hg (95% CI of 3.1-15.1)

Approach to Resistant Hypertension

3. Discontinue or Decrease Interfering Substances
### Medications That Can Interfere With Blood Pressure Control

- **Nonnarcotic analgesics**
  - Nonsteroidal anti-inflammatory agents, including aspirin
  - Selective COX-2 inhibitors, ? acetaminophen
- Sympathomimetic agents (decongestants, diet pills, cocaine, caffeine)
- Stimulants (methylphenidate, dexamethylphenidate, dextroamphetamine, amphetamine, methamphetamine, modafinil)
- Glucocorticosteroids
- **Alcohol**
- **Oral contraceptives**
  - Cyclosporine, tacrolimus
  - Erythropoietin
  - Natural licorice
  - Herbal compounds (ephedra or ma huang)

NSAIDs

Over 33 million U.S. citizens consuming NSAIDs on a regular basis. Annual sales are exceeding $12 billion.

COX-2

PGE₂

Impaired vasodilatation

Prostacyclin

Sodium retention and increase in intravascular volume

MAP increase ~ 3-5mmHg

White WB. Hypertension. 49: 408-418, 2007
NSAIDs and Blood Pressure

Amlodipine: 5-10mg/day; Lisinopril/HCTZ; (10/6.25-20/12.5 mg o.d.
Ibuprofen: 600-800 mg tid; Piroxicam: 10-20 mg/day
Acetaminophen: 1000 mg tid

Aspirin and Blood Pressure

Low dose ASA (75mg daily) for CAD prophylaxis was not reported to rise BP in Hypertension Optimal Treatment (HOT) Study (>18,000 patients)

Zanchetti A. J Hypertens. 2002;20(5):1015
Approach to Resistant Hypertension

4. Screen for Secondary Causes of Hypertension
Secondary Causes of Resistant HTN

- **Common:**
  - Obstructive Sleep Apnea
  - Chronic Kidney Disease
  - Renal Vascular Hypertension
  - Primary Hyperaldosteronism

- **Uncommon:**
  - Pheochromocytoma
  - Cushings’s Syndrome
  - Thyroid Disease
  - Primary hyperparathyroidism
  - Aortic Coarctation
  - Brain Tumors
Secondary Causes of Resistant HTN

• Screening for secondary causes should be guided by:
  - clinical history
  - physical examination
  - initial laboratory testing
  - presence of risk factors

• Current guidelines support referral to a specialist at this point even without initial screening

Approach to Resistant Hypertension

5. Pharmacological Treatment
Antihypertensive Drugs

- Calcium-channel blockers
  - Hydralazine
  - Minoxidil

- Autoregulation

- Humoral
  - ACE-inhibitors
  - Angiotensin II-receptor blockers
  - Direct renin inhibitors
  - Mineralocorticoid receptor blockers

- Salt and Water

- SNS
  - α-blockers
  - β-blockers
  - α₂-agonist

- Diuretics
Common Treatment Errors

• Doses too low (failure to titrate to effective dose)
• Inappropriate antihypertensive drug combinations
• Use of short acting drugs
• Failure to utilize diuretics when volume overload is present
  - failure to use furosemide when eGFR<40 ml/min/m$^2$
Anglo-Scandinavian Cardiac Outcomes Trial

Spironolactone 25-50mg

- CCB
- ACEI
- α-Bl

Spironolactone effectively reduced BP when added as 4th line therapy

ΔSBP = 21.9 mmHg
95% CI 20.8-23

ΔDBP = 9.5 mmHg
95% CI 9.0-10.1

Addition of Spironolactone in Patients With Resistant Arterial Hypertension (ASPIRANT)
A Randomized, Double-Blind, Placebo-Controlled Trial

Jan Václavík, Richard Sedláčk, Martin Plachý, Karel Navrátil, Jiří Plášek, Jiří Jarkovský, Tomáš Václavík, Roman Husár, Eva Kociánová, Miloš Táborský

(Hypertension. 2011;57:1069-1075.)
Addition of Spironolactone in treatment of Resistant Hypertension

Office and 24-hr ABPM at the beginning of study

Spironolactone
Placebo

Office and 24-hr ABPM at the beginning of study

BP drop from baseline, mmHg

(Hypertension. 2011;57:1069-1075.)
Is there factor(s) related to the treatment itself that contribute to unsuccessful treatment?

- Pressor response to antihypertensive drugs: increase in SBP ≥ 10mmHg

Physiology of Blood Pressure

Tissue Blood Flow and, therefore, Delivery of nutrients and Removal of metabolic products

Dual volume-vasoconstriction conception of long-term BP control

Body Sodium-Volume content $V$

Plasma Renin-ATII Vasoconstriction $R$

BP and Plasma Renin Activity (PRA)

- Normal BP: any PRA is accompanied by reciprocal changes in V
- Hypertension: kidney fail to reduce PRA in response to an increase in body salt:
  - PRA could be already maximally suppressed (low renin HTN)
  - PRA “too high” (not necessary higher than normal) for the concurrent body salt content (normal and high renin HTN)
Relationship between PRA and Sodium Intake

Normal Subjects

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Assays</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance-Outpatient</td>
<td>19</td>
</tr>
<tr>
<td>Balance-Metabolic ward</td>
<td>14</td>
</tr>
<tr>
<td>Random sample</td>
<td>20</td>
</tr>
</tbody>
</table>

Low PRA < 0.65 ng/ml/min
Medium PRA 0.65-6.5 ng/ml/min
High PRA > 6.5 ng/ml/min

Antihypertensive Drugs

Autoregulation → BP → Salt and Water → The Anti-V drugs
Humoral → BP → SNS → The Anti-R drugs
BP = V x R

The anti- V Drugs

Aldosterone-antagonists
Diuretics
Calcium-channel blocker
α₁-blockers

BP

The anti- R Drugs

R1: Block or suppress plasma renin-ATII activity:
Direct Renin blockers
ACE-inhibitors
ARB

R2: suppress renin secretion:
β-blockers
α₂-agonists

BP response based on Plasma Renin Activity and anti-V or –R drug


Plasma Renin Activity Predicts Blood Pressure Responses to β-Blocker and Thiazide Diuretic as Monotherapy and Add-On Therapy for Hypertension

- Randomized controlled trial
- 365 participants with stage I-II HTN
- Outcomes:
  1. Home BP averages before and after each drug administration
  2. Predictors of BP response such as age, race, PRA

Turner ST et al. Am J Hypertens. 23(9): 1014–1022, 2010
PRA-guided treatment of resistant hypertension

BP uncontrolled on > 3 drugs
BP controlled on > 4 drugs

Step 1: Reduce drugs to 1 anti-V and 1 anti-R

BP uncontrolled

Step 2: Measure PRA

PRA < 0.65
There is no renin to block. Anti-R may be a pressor

Step 3: stop anti-R

PRA 0.65-6.5
Renin is effectively blocked

Step 3: add 2nd anti-V

PRA >6.5
Volume depletion may be present

Step 3: stop anti-V

BP controlled, test stopping anti-V if PRA is high, or anti-R if PRA is low

Step 4: if BP uncontrolled, add 2nd anti-V drug

Step 4: if BP uncontrolled, test stopping anti-R

Step 4: if BP uncontrolled, add 2nd anti-R drug

Plasma Renin Test–Guided Drug Treatment Algorithm for Correcting Patients With Treated but Uncontrolled Hypertension: A Randomized Controlled Trial

Brent M. Egan, Jan N. Basile, Shakaib U. Behrman, Phillip B. Davis, Curt H. Grob III, Jessica Flynn Riehle, Christine A. Walters, Daniel T. Lackland, Carmen Merali, Jean E. Sealey, and John H. Laragh

Table 3 | BP and medication number at first and last visits and changes in BP and medication number between the baseline and last visits in RTGT and CHSC patients

<table>
<thead>
<tr>
<th></th>
<th>RTGT</th>
<th>CHSC</th>
<th>P value (between groups)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline BP</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>157.0 ± 2.6</td>
<td>153.2 ± 2.3</td>
<td>0.27</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>87.1 ± 2.0</td>
<td>91.1 ± 2.0</td>
<td>0.17</td>
</tr>
<tr>
<td>BP meds, N</td>
<td>3.1 ± 0.3</td>
<td>2.7 ± 0.2</td>
<td>0.21</td>
</tr>
<tr>
<td><strong>Last visit BP</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>127.9 ± 2.3*</td>
<td>134.0 ± 2.8*</td>
<td>0.10</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>73.1 ± 1.8*</td>
<td>79.8 ± 1.9*</td>
<td>0.01</td>
</tr>
<tr>
<td>BP meds, N</td>
<td>3.1 ± 0.2</td>
<td>3.0 ± 0.2</td>
<td>0.73</td>
</tr>
<tr>
<td><strong>Change BP (last–baseline)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>-29.1 ± 3.2*</td>
<td>-19.2 ± 3.2*</td>
<td>0.03</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>-14.1 ± 1.9*</td>
<td>-11.3 ± 2.0*</td>
<td>0.32</td>
</tr>
<tr>
<td>BP meds, N</td>
<td>0.0 ± 0.2</td>
<td>0.3 ± 0.1</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Values = mean ± s.e.m.
Devise-Based treatments of Resistant Hypertension

• Renal sympathetic denervation
• Baroreflex sensitization (Carotid baroreceptor stimulation)
Renal Sympathetic Activation in Hypertension

Renal nerves and the SNS
Afferent renal sympathetics

The kidney is a source of central sympathetic drive in hypertension, heart failure, chronic kidney disease, and ESRD

ESRD = end-stage renal disease; GFR = glomerular filtration rate; RBF = renal blood flow; SNS = sympathetic nervous system

Schematic illustration of the percutaneous catheter-based denervation

Norepinephrine Spillover after Renal-Nerve Ablation

Primary end-point: change in office SBP after 6-months of follow up without changes in BP medications

# SIMPLICITY HTN-2 Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Renal denervation group (n=52)</th>
<th>Control group (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline systolic blood pressure (mm Hg)</strong></td>
<td>178 (18)</td>
<td>178 (16)</td>
</tr>
<tr>
<td><strong>Baseline diastolic blood pressure (mm Hg)</strong></td>
<td>97 (16)</td>
<td>98 (17)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>58 (12)</td>
<td>58 (12)</td>
</tr>
<tr>
<td><strong>Sex (female)</strong></td>
<td>18 (35%)</td>
<td>27 (50%)</td>
</tr>
<tr>
<td><strong>Race (white)</strong></td>
<td>51 (98%)</td>
<td>52 (96%)</td>
</tr>
<tr>
<td><strong>Body-mass index (kg/m²)</strong></td>
<td>31 (5)</td>
<td>31 (5)</td>
</tr>
<tr>
<td><strong>Type 2 diabetes</strong></td>
<td>21 (40%)</td>
<td>15 (28%)</td>
</tr>
<tr>
<td><strong>Coronary artery disease</strong></td>
<td>10 (19%)</td>
<td>4 (7%)</td>
</tr>
<tr>
<td><strong>Hypercholesterolaemia</strong></td>
<td>27 (52%)</td>
<td>28 (52%)</td>
</tr>
<tr>
<td><em><em>eGFR</em> (mL/min per 1.73 m²)</em>*</td>
<td>77 (19)</td>
<td>86 (20)</td>
</tr>
<tr>
<td><em><em>eGFR</em> 45-60 mL/min per 1.73 m²</em>*</td>
<td>11 (21%)</td>
<td>6 (11%)</td>
</tr>
<tr>
<td><strong>Serum creatinine (µmol/L)</strong></td>
<td>91 (25)</td>
<td>78 (18)</td>
</tr>
<tr>
<td><strong>Urine albumin-to-creatinine ratio (mg/g)</strong> †</td>
<td>128 (363)</td>
<td>109 (254)</td>
</tr>
<tr>
<td><strong>Cystatin C (mg/L)</strong> ‡</td>
<td>0.9 (0.2)</td>
<td>0.8 (0.2)</td>
</tr>
<tr>
<td><strong>Heart rate (bpm)</strong></td>
<td>75 (15)</td>
<td>71 (15)</td>
</tr>
<tr>
<td><strong>Number of antihypertension medications</strong></td>
<td>5.2 (1.5)</td>
<td>5.3 (1.8)</td>
</tr>
<tr>
<td><strong>Patients on hypertension medication for more than 5 years</strong></td>
<td>37 (71%)</td>
<td>42 (78%)</td>
</tr>
<tr>
<td><strong>Patients on five or more medications</strong></td>
<td>35 (67%)</td>
<td>31 (57%)</td>
</tr>
<tr>
<td><strong>Patients receiving (drug class)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors/ARBs</td>
<td>50 (96%)</td>
<td>51 (94%)</td>
</tr>
<tr>
<td>Direct renin inhibitors</td>
<td>8 (15%)</td>
<td>10 (19%)</td>
</tr>
<tr>
<td>β blockers</td>
<td>43 (83%)</td>
<td>37 (69%)</td>
</tr>
<tr>
<td>Calcium-channel blockers</td>
<td>41 (79%)</td>
<td>45 (83%)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>46 (89%)</td>
<td>49 (91%)</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>9 (17%)</td>
<td>9 (17%)</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>8 (15%)</td>
<td>9 (17%)</td>
</tr>
<tr>
<td>α-1 blockers</td>
<td>17 (33%)</td>
<td>10 (19%)</td>
</tr>
<tr>
<td>Centrally acting sympatholytics</td>
<td>27 (52%)</td>
<td>28 (52%)</td>
</tr>
</tbody>
</table>

*Simplicity-2. Lancet. 376:1903-1909, 2010*
SIMPLICITY HTN-2: Outcomes

Mean Systolic and diastolic BP changes from baseline after renal denervation with up to 2 yrs of follow up

Carotid Baroreceptor Stimulation

- This method uses a novel implantable device (Rheos System, CVRx, Inc., Minneapolis, Minnesota) that works by electrical stimulation of the carotid sinus
- A nonrandomized prospective study (n=45) to assess whether Rheos therapy could safely lower blood pressure in patients with resistant hypertension

<table>
<thead>
<tr>
<th></th>
<th>3 Months</th>
<th>1 Year</th>
<th>2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office blood pressure</td>
<td>n = 37</td>
<td>n = 26</td>
<td>n = 17</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>−21 ± 4 (p &lt; 0.001)</td>
<td>−30 ± 6 (p &lt; 0.001)</td>
<td>−33 ± 8 (p = 0.001)</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>−12 ± 2 (p &lt; 0.001)</td>
<td>−20 ± 4 (p &lt; 0.001)</td>
<td>−22 ± 6 (p = 0.002)</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>−8 ± 2 (p &lt; 0.001)</td>
<td>−8 ± 2 (p = 0.001)</td>
<td>−11 ± 4 (p = 0.008)</td>
</tr>
</tbody>
</table>

6. Refer to hypertension specialist
Specialist in Clinical Hypertension

- Certification is offered by American Society of Hypertension
- 3 subspecialties qualify: Cardiology, Nephrology, and Endocrinology
- The specific purpose is to identify and recognize physicians with expert skills and knowledge in the management of clinical hypertension and related disorders.
- These physicians can act as local and regional consultants for the more complex and difficult cases and also assist in advice regarding guidelines and process improvement.
- Specialist Directory: www.ash-us.org
Specialist Referral

- Indications to referral:
  1. Refer to appropriate specialist for known or suspected secondary cause(s) of hypertension
  2. Refer to hypertension specialist if BP remains uncontrolled after 6 months of treatment
Conclusions

• Uncontrolled HTN ≠ Resistant HTN
• Exclusion of pseudoresistance, implementation of life-style interventions, and discontinuation of interfering substances are initial steps in approaching resistant HTN
• Work up for secondary causes of resistant hypertension should be reserved for patients with appropriate clinical clues
• Referral to hypertension specialists can help to improve BP control
CASE PRESENTATION

62 years-old female was referred to you for the evaluation and treatment of difficult to control HTN. Her BP is >140/90 in PCP office for several times while taking daily HCTZ 25 mg, Lisinopril 40 mg, and Amlodipine 10 mg. ROS is + for occasional headaches for which she takes “pain killers”. She works as a manager in a local grocery store. On exam, BMI 35 kg/m2, HR 94, BP 164/103. +pitting edema in both ankles. Laboratory findings are significant for glucose 92 mg/dl, K 3.7 mmol/l, Cr 1.0 mg/dL.

What is the next most appropriate step in the management of patient’s hypertension?

1. Add metoprolol 50 mg bid
2. Measure 24-hr urine free cortisol
3. Measure morning aldosterone concentration and plasma renin activity
4. Measure fractionated plasma metanephrines
5. Review medication list including OTC meds, advise to reduce Na intake, encourage 5-7% weight loss and exercise 30 mins/day, encourage to take medications daily
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THANK YOU

QUESTIONS?