Renal Denervation in the Treatment of Resistant Hypertension

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Objectives

- Resistant hypertension
  - Definition
  - Pathophysiology
  - Appropriate drug therapy
- Renal denervation therapy
  - Rationale
  - Procedure
  - Effectiveness

Resistant Hypertension

- Resistant HTN is NOT synonymous with uncontrolled HTN
- Resistant HTN- BP above goal despite therapy with ≥ 3 drugs from different classes at full doses, one of which is a diuretic
- Pseudoresistant HTN- 
  - Poor technique
  - Pseudohypertension
  - Poor compliance with meds
• 468,877 patients with HTN
  – 147,635 (31.5%) were uncontrolled
    • Among uncontrolled, 44,684 were prescribed ≥ 3 medications (30.3%)
    • 102,951 were prescribed appropriate medications (19%)
• Pharmacists’ role
  – Check BP at pharmacy
  – Instruct patient on home BP monitoring
  – Assess medication regimen for appropriateness
  – Stress compliance
  – Reinforce therapeutic lifestyle changes

Lifestyle Changes
• Smoking Cessation
  • Does not lower BP
  • Decrease in CV risk occurs in about 3 years
• Alcohol Consumption
  • Linear relationship between alcohol and BP
• Sodium Restriction
  • Greater effect in black patients, elderly patients, or patients with CKD
  • Recommend < 5 g of salt per day or < 1.5 g of sodium
  • Sodium is 39.34% of the weight of sodium chloride
• DASH Diet
  • High in fruits, vegetables & low-fat dairy products, low in saturated fats
• Physical Exercise & Weight Loss
  • Endurance activity 30-45 min/daily ↓ SBP 3-4 mm Hg

Potential Combinations
Factors Contributing to Resistance

- Discontinue or minimize medications that may increase BP (NSAIDs)
- Identify any lifestyle factors
  - Excessive alcohol
  - Excessive salt
- Evaluate renal function
- Rule out secondary HTN

Polycystic Kidney Disease

Renal Artery Stenosis

- Renal artery supplies blood flow to kidneys
- Renal artery stenosis occurs when there is partial blockage of the artery typically caused by atherosclerosis
Fibromuscular Dysplasia

• 2nd leading cause of renal artery stenosis

• Hyperplastic disorder that affects medium-size and small arteries

• Characterization:
  – Heterogenous group of lesions
  – Fibrous or fibromuscular thickening

Adrenal Glands

• Endocrine gland

• Located on each kidney

• Composed of:
  – Adrenal medulla
  – Adrenal cortex

• Function to secrete essential hormones into the blood
Adrenal Cortex

• Secretes steroid hormones:
  – Aldosterone
  – Cortisol
  – Corticosterone
  – Dehydroepiandrosterone (DHEA)
  – Androstenedione

Causes of Mineralocorticoid Excess

• Primary hyperaldosteronism
  – Adrenal (Conn’s) adenoma:
    • Mechanism: autonomous aldosterone excess
  – Bilateral (micronodular) adrenal hyperplasia:
    • Mechanism: autonomous aldosterone excess

• Hyperaldosteronism
  – Plasma aldosterone levels may be higher than in patients with primary hyperaldosteronism!
Aldosterone Blockade Dosing

• Genomic (natriuretic) effects
  • Spironolactone 100 to 400 mg/day
  • Eplerenone 50 to 100 mg/day

• Nongenomic (non-natriuretic) effects
  • Spironolactone 25 to 50 mg/day
  • Eplerenone 50 mg/day

Obstructive Sleep Apnea

• Characterized by partial or complete closure of the upper airway, posterior from the nasal septum to the epiglottis, during inspiration

Obstructive Sleep Apnea

• Prevalence:
  – HTN present in >50% of patients with OSA
• Risk factor:
  – Obesity (70% of patients with OSA are obese)
• Consider in patients with:
  – Drug-resistant hypertension
  – History of snoring
The sympathetic nervous system (SNS) is a major contributor to HTN through its effects on sodium and water retention, increased renin release, and alterations in blood flow.
Renal Nerves in HTN

- Kidneys have a dense afferent sensory and efferent sympathetic innervation.
- Renal sensory afferent nerve activity directly influences sympathetic outflow to the kidneys and organs involved in cardiovascular control.

Rationale for RSDN

- Access to the renal artery is obtained through the femoral artery
- A renal angiogram is performed to rule out renal artery stenosis
- A treatment catheter is introduced into the renal artery
- Low energy radiofrequency ablations are applied to each renal artery
Anticoagulation & Antiplatelet Therapy

- Patients should be anticoagulated prior to the procedure to prevent possible thrombus formation
- ASA 250 mg during the procedure and 75 to 100 mg daily for 4 weeks after RSDN is recommended

Assessment of Efficacy

- BP rarely changes immediately after the procedure
- Often takes weeks or months for BP reductions to occur
- Exact mechanism for BP reduction not known but could relate to:
  - Decrease sympathetic activation
  - Decrease total peripheral resistance
  - Decrease renin release
  - Alterations in sodium and water handling
Eligible patients:
- Adults 18 to 85 years with SBP ≥ 160 mm Hg despite ≥ 3 HTN meds

Intervention:
- Randomized to renal denervation using the Symplicity system (52 patients) or control (54 patients)
- Control group patients were allowed to cross over at 6 months if SBP ≥ 160 mm Hg

Primary outcome:
- Change in office BP at 6 and 12 months

Results

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<thead>
<tr>
<th></th>
<th>Group (n=52)</th>
<th>Group (n=54)</th>
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</thead>
<tbody>
<tr>
<td>BP before procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>178.3±18.2</td>
<td>180.9±18.6</td>
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<tr>
<td>DBP, mm Hg</td>
<td>96.5±15.5</td>
<td>98.6±15.5</td>
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<tr>
<td>6 min after procedure</td>
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<tr>
<td>SBP, mm Hg</td>
<td>146±23.3</td>
<td>150.3±24.7</td>
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<tr>
<td>DBP, mm Hg</td>
<td>84.4±17.9</td>
<td>91.3±14.9</td>
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<td>12 min after procedure</td>
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<tr>
<td>SBP, mm Hg</td>
<td>150.2±21.9</td>
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<tr>
<td>DBP, mm Hg</td>
<td>67.0±16.1</td>
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A Controlled Trial of Renal Denervation for Resistant Hypertension

Eligible patients:
- Adults with SBP ≥ 160 mm Hg despite ≥ 3 HTN meds
- 24-hour ambulatory systolic blood pressure ≥ 135
- 2 out of 3 patients were excluded prior to randomization because SBP < 160 mm Hg after meds were optimized

Intervention:
- Randomized to renal denervation using the Symplicity system or sham procedure

Primary outcome:
- 15 mmHg reduction in office systolic blood pressure at 6 months
RSDN

• Implications:
  – Study design of Symplicity HTN-3 was more rigorous than Symplicity HTN-2
    • Used a sham-control group
    • Greater exposure to spironolactone
  – The biology behind renal denervation is compelling but until convincing data are available, the use of RSDN should be reserved for clinical trials

Conclusions

• Optimize medical therapy
  – ? Spironolactone
• Reinforce therapeutic lifestyle changes
• Rule out secondary causes of HTN
• If home blood pressure monitoring and office SBPs are > 160 mm Hg, refer to HTN specialist
Selected References