Resistant Hypertension, Sleep Apnea and Hyperaldosteronism

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Faculty Disclosure

• Medtronic: Grant Support
Resistant Hypertension

Blood pressure that remains uncontrolled with use of 3 antihypertensive agents. Ideally one of the agents should be a diuretic and all agents should be prescribed at doses to provide optimal benefit.

Prevalence of Resistant Hypertension in US
NHANES 1988-2008

Roberie and Elliot, Curr Opinion Cardiol, in press
Prevalence of Primary Aldosteronism in Subjects With Resistant Hypertension

Seattle: 17%
Birmingham: 20%
Oslo: 22%
Prague: 19%


High Prevalence of Unrecognized Sleep Apnoea* in Drug-Resistant Hypertension

Logan et al. J Hypertens 2001;19:2271

* >10 events/hr
Prevalence of OSA

Middle-Aged Adults\(^1\)
Hypertension\(^2\)
Resistant Hypertension\(^3\)

\(^1\)Young et al. NEJM 1993. AHI \(\geq 5\) events/hr.
\(^3\)Logan et al. J Hypertens 2001. AHI \(\geq 10\) events/hr.

Sleep Apnea Syndrome: A Possible Contributing Factor to Resistant Hypertension

<table>
<thead>
<tr>
<th>BP Uncontrolled</th>
<th>BP Controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m(^2))</td>
<td>33.7</td>
</tr>
<tr>
<td>Neck (cm)</td>
<td>43.5</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>1.00</td>
</tr>
<tr>
<td>AHI (events/hr)</td>
<td>44</td>
</tr>
<tr>
<td>HI (%)</td>
<td>36</td>
</tr>
</tbody>
</table>

Lavie and Hoffstein. Sleep 2001;24:721
CPAP in Patients with Resistant Hypertension

Logan et al, Euro Respir Care 2003

Aldosterone Levels and Risk of OSA in Subjects with Resistant Hypertension

Calhoun et al. CHEST 2003
Study Protocol

Subjects with Resistant Hypertension and Control Subjects without Resistant Hypertension

Plasma aldosterone, renin level, 24-hour urine for aldosterone and creatinine

Full-night diagnostic polysomnogram

Biochemical and polysomnography results of evaluated subjects with resistant hypertension (n=71)* and without resistant hypertension (n=29)*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Resistant Hypertension</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAC, ng/dL</td>
<td>12.4±7.9</td>
<td>7.3±3.6</td>
</tr>
<tr>
<td>PDR, µUnits/mL</td>
<td>21.4 ± 36.0</td>
<td>27.6±29.7</td>
</tr>
<tr>
<td>Serum Cr, mg/dL</td>
<td>1.1 ± 0.3</td>
<td>1.0</td>
</tr>
<tr>
<td>Serum K, mEq/L</td>
<td>3.8 ± 0.4</td>
<td>4.3</td>
</tr>
<tr>
<td>AHIL, events/hr</td>
<td>24.1±24.7</td>
<td>29.0±32.3</td>
</tr>
<tr>
<td>HI, %</td>
<td>7.4±10.9</td>
<td>2.9±3.8</td>
</tr>
<tr>
<td>OSA Prevalence</td>
<td>85%</td>
<td>83%</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD.
†Different from resistant hypertension subjects (p < 0.05).
Apnea-hypopnea index and hypoxic index correlates with plasma aldosterone in resistant hypertension subjects

Figure 1

Apnea-hypopnea index and hypoxic index does not correlate with plasma aldosterone in control subjects

Figure 2

Rho = 0.44, p = 0.0002

Rho = 0.38, p = 0.001

Rho = 0.12, p = 0.52

Rho = 0.002, p = 0.99
Serum and 24-hr Urinary Aldosterone Related to Severity of OSA in Patients with Resistant Hypertension and Hyperaldosteronism

Gonzaga et al., J Clin Sleep Med 2009

PATIENTS WITH RESISTANT HYPERENSIION AND OSA

NORMAL ALDOSTERONE

HIGH ALDOSTERONE

Gonzaga et al., J Clin Sleep Med 2009
**Results**

Sim J et al, J Hypertens, 2011

Gaddam et al, J Human Hypertens 2009

AHI, Apnea-Hypopnea Index; HI, Hypoxic Index; REM, Rapid eye movement sleep; * p<0.05.
BNP and ANP Levels in Patients with Resistant Hypertension vs. Control Subjects

Gaddam et al., Arch Intern Med 2008

BNP and ANP Levels in Patients with High and Normal Aldosterone and Resistant Hypertension vs. Control Subjects

Gaddam et al., Arch Intern Med 2008
Neck Circumference and Upper Airway Resistance After Lower Body Positive Pressure

Lower body positive pressure (filled squares)

Controls (open squares)

Chiu et al, Am J Respir Crit Care Med 2006

Change in AHI in Patients with CHF Exacerbation after Diuresis

Bucca et al, CHEST 2007
Effect of 8-12 Weeks of CPAP Use in Hypertensive Patients with OSA

### All Subjects (n=24)
Mean CPAP Use 2.2 hr/night

### CPAP Compliant (n=12)
Mean CPAP Use 5.4 hr/night

Acelajado et al, submitted

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Change after CPAP</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma aldosterone (ng/ml)</td>
<td>-0.70 ± 5.74</td>
<td>0.562</td>
</tr>
<tr>
<td>Plasma renin activity (ng/ml/hr)</td>
<td>0.74 ± 5.48</td>
<td>0.533</td>
</tr>
<tr>
<td>Urinary aldosterone (µg/24 hours)</td>
<td>-1.02 ± 4.55</td>
<td>0.317</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>-0.77 ± 18.07</td>
<td>0.830</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>-1.35 ± 10.83</td>
<td>0.532</td>
</tr>
<tr>
<td>Urinary cortisol (µg/24 hours)</td>
<td>0.96 ± 72.63</td>
<td>0.948</td>
</tr>
</tbody>
</table>

### Resistant Hypertension
High/Low Dietary Salt Cross-Over Evaluation

Pimenta et al. Hypertension 2009
**Results: High-Low Salt Cross-Over**

<table>
<thead>
<tr>
<th></th>
<th>High-salt (n=12)</th>
<th>Low-salt (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>94.3±18.6</td>
<td>92.7±17.6*</td>
</tr>
<tr>
<td><strong>BNP (pg/mL)</strong></td>
<td>35.1±32.1</td>
<td>12.5±10.8*</td>
</tr>
<tr>
<td><strong>Serum K (mEq/L)</strong></td>
<td>3.8±0.3</td>
<td>4.1±0.5</td>
</tr>
<tr>
<td><strong>PAC (ng/dL)</strong></td>
<td>11.1±4.8</td>
<td>15.5±9.3*</td>
</tr>
<tr>
<td><strong>PRA (ng/mL/h)</strong></td>
<td>0.9±0.5</td>
<td>14.3±32.6</td>
</tr>
<tr>
<td><strong>Ualdo (mcg/24-hr)</strong></td>
<td>11.7±5.1</td>
<td>18.6±11.2*</td>
</tr>
<tr>
<td><strong>UK (mEq/24-hr)</strong></td>
<td>56.9±21.8</td>
<td>69.2±27.7*</td>
</tr>
<tr>
<td><strong>UNa (mEq/24-hr)</strong></td>
<td>261.5±70.4</td>
<td>48.6±27.2*</td>
</tr>
<tr>
<td><strong>TFC (kohms⁻¹)</strong></td>
<td>29.3±3.7</td>
<td>26.5±3.5</td>
</tr>
</tbody>
</table>

* Different from high-salt, p<0.05  

Pimenta et al. Hypertension 2009

**Reduction in Blood Pressure High to Low Salt Ingestion**

- Office: -23 mmHg  
- Daytime: -21 mmHg  
- Nighttime: -20 mmHg  

Systolic □ Diastolic

Pimenta, HYPERTENSION, 2009
Dietary Salt Related to Severity of Sleep Apnea in Patients with Resistant Hypertension

Kasai et al, JACC, 2011

RENAL DENERVATION – SIMPLICITY HTN-2 TRIAL

Baseline BP=178/97 mm Hg on 5.2 medications

METABOLIC EFFECTS OF RENAL DENERVATION
Effects of Renal Sympathetic Denervation on Blood Pressure, Sleep Apnea Course, and Glycemic Control in Patients With Resistant Hypertension and Sleep Apnea

Adam Witkowski, Aleksander Przybysz, Elżbieta Florczak, Jacek Kądziela, Paweł Śliwiński, Piotrnowski Biekoł, Irena Michalkowska, Marek Kubat, Ewa Warchol, Magdalena Janiszewicz, Krzysztof Narkiewicz, Virend K. Somers, Paul A. Sobota, Andrzej Jamszewicz

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