Challenges to Manage Blood Pressure in ESRD and Heart Failure Patients

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Case Presentation

- 65 year old male
  - Diabetes with retinopathy and neuropathy
  - Ischemic cardiomyopathy with EF

Pre-HD
- Inter-dialytic weight gain: 3.5 kg
- Sitting BP: 180/96 mmHg
- Standing: 140/80 mmHg
- JVD 10 cmH2O
- Lungs: no rales
- CVS: Regular, normal sounds, 1+ b/l peripheral edema

Intra-dialysis
- 30 min: UF = 500 cc
- 60 min: UF = 1000 cc with headache

Medications
- Carvedilol 12.5 mg bid
- Losartan 50 mg daily
- Isosorbide dinitrate
- Aspirin, statin
- Warfarin

Action Plan
- ↓ both BB and ARB
- Reemphasized to reduce IDWG
- ↓ dialysate temperature to 36C
- Increased dialysis time
- Started Midodrin 5 mg at 0-30 min into dialysis

Cardiology/PCP clinic
- Sitting BP: 150/90 mmHg
- Medication list: minimal dose of BB and ARB, and !! Midodrin
- Increase in BB or ARB or addition of 4th med

Challenges in BP Management
- Hypertension
  - Pre-HD
  - Interdialytic
- Hypotension
  - On dialysis
- Orthostatic hypotension
  - Worse post-HD
  - Inter-dialytic

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BP Pattern In A Hemodialysis Patient Over A Week


BP Pattern in A Peritoneal Dialysis Patient Over Days

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Pathogenesis: **HYPERTENSION**

**Volume Overload**
- Expanded extracellular fluid volume
- Increased sympathetic activity
- Increased renin-angiotensin system activity

**Failure to suppress vasoconstrictor system**
- ↓ NO production by endothelium
- ↑ Asymmetric Dimethyl Arginine (ADMA)

**Impaired vasodilatation**
- Reversing of hypoxia induced vasodilatation
- Increased viscosity
- Activation of neurohormones

**Erythropoietin**
- ↓ Entry of calcium into vessel smooth muscle cells

**Secondary Hyperparathyroidism**
- ↑ Entry of calcium into vessel smooth muscle cells

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**Diagnosis of Hypertension**

- **Ideal:** Ambulatory or Home BP monitoring
- **Next best is Average of pre-HD, post-HD, and intra-dialytic BP**
- **Hypertension = SBP>130/80**

Management of Hypertension

• Achieving euvolemia
  – Dietary sodium restriction
  – Challenge dry weight: may not have visible edema till 3-4 lt ECF excess
    • Increase ultrafiltration
      – Increase time
      – Addition of sessions
    • Lower sodium dialysate

• Achieving euvolemia
• Achieving euvolemia
• Assessment of dry weight
  – Crit-line
  – Bio-impedence analysis
  – needs further refinement before being used in the clinic

Pharmacological Interventions for Hypertension

• Beta blockers are the first choice
  – RCT: mortality benefit
  – Observation studies reporting decreased sudden death
• ACEI and CCB
  – Reduced CVD
• Spironolactone
  – Reduced CVD and all-cause mortality

Cice et al. (J Am Coll Cardiol 2003;41:1438–44)  
Hypotension In Dialysis Patients

- **Acute (episodic) hypotension**: Sudden drop in SBP
  - To < 90 mmHg or
  - Change > 20mmHg with accompanying clinical symptoms
  - Intra-dialytic sessions
- **Recurrent**: Minimum 50% of dialysis sessions
- **Chronic**: Persistent SBP <90–100 mmHg
- **Orthostatic hypotension**: >20 mmHg drop on standing
- **Prevalence**
  - Acute: 15-30% in ESRD population
    - >50% in diabetic and elderly
  - Chronic: 3-5% patients


Pathogenesis of Hypotension in Dialysis Patients

- **Aggressive Ultrafiltration**
  - Reduction in intravascular volume
  - Refilling from the interstitium/sometimes ICF
  - Increased cardiac output
  - Increased SVR X
  - Normal heart and normal baro-autonomic system/baro-reflexes X

\[ \text{BP} = \text{CO} \times \text{SVR} \]
Normal Autonomic System

Decrease in Intra-arterial Volume
- Venous pooling on standing
- Removal through dialysis

Stimulation of Baroreceptors

↑ Sympathetic Discharge

Increase CO
- ↑ HR
- ↑ Contractility

Maintain the Blood Pressure

True hypovolemia: these responses not enough → hypotension with tachycardia

Autonomic Failure: not much responses → hypotension with no change in heart rate

Other Causes for Failure to Compensate for Vascular Underfilling

- Severe cardiovascular disease
  - Systolic heart failure
  - Diastolic dysfunction – unable to raise stroke volume
  - Right heart failure causing impaired left heart filling
  - Pericardial effusion
- Impaired Systemic vascular resistance
  - Liver disease
  - Calcified stiff blood vessels
  - Impaired vasopressin response
- Autonomic dysfunction
  - Diabetes
  - Uremia
  - Elderly with poor baroreceptor sensitivity
Infrequent Causes of Hypotension

- **Endocrine**: more associated with chronic
  - Hypothyroidism
  - Adrenal insufficiency
- **Dialysis related factors**
  - Low Na or Ca or high Mg dialysate
  - Non-biocompatible membrane

Management of Hypotension

- **Avoid Aggressive Ultrafiltration**
  - Decrease inter dialytic weight gain
    - Dietary salt restriction
    - DO NOT CONCENTRATE ON FLUID RESTRICTION
  - Decrease UF rate
    - Increase dialysis time
  - Additional dialysis sessions
Management of Hypotension (contd.)

- **Cardiac work up:** ECHO, Cards consult
  - **Cardiac Intervention**
    - Ischemic: revascularization
    - Valvular disease: surgical or percutaneous repair
    - Remodeling: Beta-blockers and Angiotensin blockers
    - Removal of excess volume

  - Liver
  - Autonomic Failure
  - Cardiac Intervention

  - Increase systemic vascular resistance
    - Cooling of dialysate
    - α-1 receptor agonist like midodrine

Autonomic Failure in Dialysis Patients

- **Etiology**
  - Aging
  - Diabetes
  - Uremia

- **Pathogenesis**
  - Autonomic neuropathy - small fiber damage
    - Both sympathetic and parasympathetic
  - Decrease neuronal storage of adrenaline
  - Reduced baroreceptor sensitivity

- **Prevalence**
  - 50% of maintenance dialysis patients

Savica et al. Am J of Kidney Dis 2001: 38, No 4, Suppl 1 (October); pp S118-S121
Autonomic Insufficiency

**Autonomic Function Tests**

<table>
<thead>
<tr>
<th>Group (n)</th>
<th>Amyl Nitrite</th>
<th>Valsalva Maneuver (Release phase)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Δ MAP (mmHg)</td>
<td>Δ HR (bpm)</td>
</tr>
<tr>
<td>Normal (6)</td>
<td>-44</td>
<td>43</td>
</tr>
<tr>
<td>Uremia 1 (2)</td>
<td>-45</td>
<td>47</td>
</tr>
<tr>
<td>Uremia 2 (6)</td>
<td>-51</td>
<td>6</td>
</tr>
<tr>
<td>Heart failure (6)</td>
<td>-17</td>
<td>4</td>
</tr>
</tbody>
</table>

**Changes during hemodialysis**

<table>
<thead>
<tr>
<th>Group</th>
<th>Δ MAP (mmHg)</th>
<th>Δ HR</th>
<th>Δ SVR</th>
<th>Blood Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uremia 1 (2)</td>
<td>-34</td>
<td>+11</td>
<td>+2.1</td>
<td>-0.4</td>
</tr>
<tr>
<td>Uremia 2 (6)</td>
<td>-69</td>
<td>-3</td>
<td>-14.4</td>
<td>-0.4</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.001</td>
<td>ns</td>
</tr>
</tbody>
</table>

Kersh et al. NEJM 1974:3;650

**Hypotension due to Autonomic Failure in Hemo Vs. Peritoneal Dialysis Patients**

**Hemodialysis**

- During dialysis
- Immediate post dialysis on standing
- Less during Inter-dialytic time
  - slowly rising plasma volume
  - collection of uremic toxins

**Peritoneal Dialysis**

More in patients with co-existent heart failure and autonomic insufficiency
Effect of α-1-adrenergic Agonist During Hemodialysis

- **Midodrin**
  - Completely and rapidly absorbed
  - Peak level in 40 min
  - Elimination T1/2 – 30 min

- **De-glymidodrin**
  - Peak level in 60-90 min
  - Elimination t1/2 – 3 hours

- **In ESRD**: 10 hours
  - Dialysis removes efficiently

- **Action**
  - Arteriolar constriction: ↑SVR
  - Venoconstriction: ↑ venous return and ↑cardiac output

Concerning Effects of Midodrine

- **Cardiogenic hypotension**
  - Increase afterload and pre-load
- **Supine hypertension**
- **Persistent Hypertension**
  - If don’t achieve euvolemia
- **Peripheral vascular disease**
  - Worsening ischemia
- **Urinary retention**

Cruz et al. American Journal of Kidney Diseases 1997: 30(6);772-779
Midodrine in Patients with Heart Failure and Dialysis Associated Hypotension


Better volume status
Resolution of symptoms
Less nurses intervention

Fluid Overload Independently Associated with Worse Outcome


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Case Presentation

• 65 year old male
• Diabetes with retinopathy and neuropathy
• Ischemic cardiomyopathy with EF 30%
• Previous smoker, left BKA
• HTN and ESRD –
• Initiated hemodialysis 2 months ago mainly for volume overload symptoms

Pre-HD
• Inter-dialytic weight gain: 3.5 kg
• Sitting BP: 180/96 mmHg
• Standing: 140/80 mmHg
• JVD 10 cmH20
• Lungs: no rales
• CVS: Regular, normal sounds, 1+ b/l peripheral edema

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• 30 min: 120/86 mmHg, UF = 500 cc
• 60 min: 96/70 mmHg with headache, UF = 1000 cc

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Cardiolog/PCP clinic
• Sitting BP: 150/90 mmHg
• Medication list: minimal dose of BB and ARB
• ???Addition or increase dose of BP meds

Sitting BP: 150/90 mmHg
Standing BP: 118/82 mmHg

Sitting BP: 140/88 mmHg
Standing BP: 106/78 mmHg

Our Approach For Use of Midodrine in Autonomic Insufficiency

• Maximal efforts to reduce IDWG
  – With high UF rate- hypotension is inevitable
• Rule out cardiogenic sources requiring intervention
  – Pericardial effusion
  – Active ischemia
  – Uncorrected valvular disease
• Cardiogenic vs autonomic failure
  – Orthostatic drop less common in heart failure
  – Pure heart failure usually have chronic hypotension
• Careful with H/O Urinary retention
Our Approach For Use of Midodrine-contd.

• Hemodialysis
  – Pre-HD
  – Mid-HD if pre-HD BP is very high
  – Rarely need during interdialytic period as compensation through volume gain
• Peritoneal Dialysis
  – Need on daily basis bid to tid
  – We give parameters to the patients to hold to avoid supine hypertension
    • Sitting SBP> 150-160 mmHg
    • Standing SBP>110-120 mmHg
• Recommendation for other providers
  – Check standing BP as well

Take Home Messages

• Blood pressure fluctuates in all the ranges in ESRD patients
  – In relation to the timing of the dialysis
  – Modality
• ABPM or Home BP are the best assessment
  – In absence, average of pre-, post-HD and intradialytic BP
• Autonomic failure is common
  – Elderly diabetic
  – Orthostatic measurement of BP is of vital importance
• Volume control is important to manage both high and low BP
  – Dietary sodium restriction
  – Ultrafiltration
THNAK YOU!

Questions?