Assessment and management of symptoms in patients on dialysis

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&
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Patient presentation

- 78 y.o. WM about to start dialysis
- History of CHF, CAD
- Interested in 3x/wk HD – candidacy and interest in transplant not confirmed
This patient’s question to me was?

1) Are you going to maintain my Kt/V (measure of dialysis adequacy) > 1.2 consistently?
2) Will my hematocrit be kept between 33-36%?
3) What is the target parathyroid hormone level when I start HD?
4) How am I going to feel on hemodialysis?
Outline of talk

- Prevalence & severity of sx in ESRD
- Associations of sx with HRQoL
- Renal provider recognition of sx
- Assessment tools
- Management of pain in ESRD
Fig. 1. Frequency and occurrence of somatic symptoms in the hemodialysis and CAPD groups. *p < 0.05.
Symptom Prevalence

9-item sx survey in 226 HD and PD pts

Merkus MP et al, NDT 1999;1163-70
## Relative Symptom Burden

Based on reports of Memorial Sx Assess Scale

<table>
<thead>
<tr>
<th>Patient population</th>
<th>No. of symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysis patients with CCI ≥ 8</td>
<td>10.2 ± 5.0</td>
</tr>
<tr>
<td>Cancer out-patients$^c$</td>
<td>9.7 ± 6.0</td>
</tr>
<tr>
<td>Cancer patients$^d$</td>
<td>11.5 ± 6.0</td>
</tr>
</tbody>
</table>

Weisbord SD et al, NDT 2003;1345-52
Symptom Prevalence

30-item Dialysis Symptom Index in 162 HD pts

Weisbord SD et al – JASN 2005;2487-94
Mean Sx severity – 1 = not bothersome to 5 = very bothersome

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td>3.63</td>
</tr>
<tr>
<td>Bone/joint pain</td>
<td>3.61</td>
</tr>
<tr>
<td>Difficulty with sex arousal</td>
<td>3.44</td>
</tr>
<tr>
<td>Trouble falling asleep</td>
<td>3.35</td>
</tr>
<tr>
<td>Muscle cramps</td>
<td>3.31</td>
</tr>
<tr>
<td>Itching</td>
<td>3.24</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3.21</td>
</tr>
<tr>
<td>Nausea</td>
<td>3.16</td>
</tr>
<tr>
<td>Muscle soreness</td>
<td>3.14</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3.12</td>
</tr>
<tr>
<td>Trouble staying asleep</td>
<td>3.10</td>
</tr>
</tbody>
</table>

More than somewhat bothersome

Weisbord SD et al – JASN 2005;2487-94
Summary # 1

• Sx in patients on HD:
  – Highly prevalent
  – Similar prevalence to cancer pts
  – Frequently severe

• Relevance to our pt:
  – likely to suffer from multiple sx -> fatigue, pain, sex dysfxn, sleep disturbance
  – Many sx likely to be somewhat severe

Question → Are sx important → associated with impaired HRQoL ?
Sx & HRQoL

Davison SN et al. KI 2006; 1621-25
Sx & HRQoL – longitudinal association

Davison SN et al. NDT 2006; 3189-95
**Table 5.** Multiple regression models to explain poorer mental summary QL scores (MCS) in haemodialysis and peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Independent determinants</th>
<th>Cumulative explained variance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haemodialysis</strong></td>
<td></td>
</tr>
<tr>
<td>Lower haemoglobin</td>
<td>8</td>
</tr>
<tr>
<td>Renal vascular disease</td>
<td>11</td>
</tr>
<tr>
<td>Lower rGFR</td>
<td>14</td>
</tr>
<tr>
<td>Greater symptom burden</td>
<td>37</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>23%</td>
</tr>
</tbody>
</table>

Merkus MP et al, NDT 1999;1163-70
Table 4. Multiple regression models to explain poorer physical summary QL scores (PCS) in haemodialysis and peritoneal dialysis patients

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<tbody>
<tr>
<td>Haemodialysis</td>
<td></td>
</tr>
<tr>
<td>Medium and high comorbidity–age index</td>
<td>17</td>
</tr>
<tr>
<td>Greater age</td>
<td>22</td>
</tr>
<tr>
<td>Greater symptom burden</td>
<td>39</td>
</tr>
</tbody>
</table>

17%

Merkus MP et al, NDT 1999;1163-70
Correlations among Sx, HRQoL, and Depression \((r)\)

<table>
<thead>
<tr>
<th></th>
<th>↓ HRQoL</th>
<th>↑ depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ Sx prevalence</td>
<td>0.60</td>
<td>0.62</td>
</tr>
<tr>
<td>↑ Sx severity</td>
<td>0.61</td>
<td>0.64</td>
</tr>
</tbody>
</table>

p-value < 0.001 for all correlations

Weisbord SD et al – JASN 2005;2487-94
Summary # 2

• Sx:
  – Highly correlated with ↓ HRQoL & ↑ depression
  – Changes in sx correlate with changes in HRQoL

• Our pt:
  – Sx likely to be associated with ↓ HRQoL and ↑ depression

Question – Are sx routinely assessed and treated by renal providers?
Renal provider understanding of sx in HD pts

- Cross sectional study of 75 HD pts and 18 renal providers
- \textbf{1}^{\text{st}} \text{Hypothesis:} Renal providers not aware of sx in HD pts
- \textbf{1}^{\text{st}} \text{Aim:} To assess renal provider awareness of sx in HD pts

Weisbord SD et al. CJASN 2007; 960-67
Recruitment Methods

Consent obtained from renal providers at all three HD units

Participating provider evaluates patient during routine HD rounds

Patients seen by provider earlier in HD treatment approached to participate

DSI administered to consenting patients during HD treatment

Study provider located in HD unit and asked to complete DSI for enrolled patient
## Pt and provider Dialysis Symptom Index

### During the past week: Did you experience this symptom?

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Not At All</th>
<th>A Little Bit</th>
<th>Somewhat</th>
<th>Quite a Bit</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Constipation</td>
<td>DON’T KNOW</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

### If “yes”:

*How much did it bother you?*

<table>
<thead>
<tr>
<th>Rating</th>
<th>Not At All</th>
<th>A Little Bit</th>
<th>Somewhat</th>
<th>Quite a Bit</th>
<th>Very Much</th>
</tr>
</thead>
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<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
Methods: Analyses

• Pt-provider agreement on presence of sx → kappa statistic
• Pt-provider agreement on severity of sx → weighted kappa statistic
• Accuracy of provider reports – sensitivity, specificity, PPV, NPV
  – Pt report gold standard
Results: Provider responses

• Under-report presence of 29 of 30 sx
• “Don’t know” responses
  – 76% for “difficulty with sexual arousal”
  – 3% for SOB & 5% for swelling in legs
• Sx severity under-estimated 63% of time

Weisbord SD et al. CJASN 2007; 960-67
## Provider responses - “potentially treatable” symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>K</th>
<th>Sens</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone/joint pain</td>
<td>0.04</td>
<td>18</td>
<td>87</td>
<td>46</td>
<td>64</td>
</tr>
<tr>
<td>↓ Interest sex</td>
<td>0.01</td>
<td>6</td>
<td>98</td>
<td>50</td>
<td>77</td>
</tr>
<tr>
<td>Diff sex arousal</td>
<td>0.03</td>
<td>19</td>
<td>98</td>
<td>80</td>
<td>76</td>
</tr>
<tr>
<td>Prob fall asleep</td>
<td>0.08</td>
<td>21</td>
<td>93</td>
<td>70</td>
<td>60</td>
</tr>
<tr>
<td>Prob stay asleep</td>
<td>0.05</td>
<td>15</td>
<td>88</td>
<td>50</td>
<td>55</td>
</tr>
<tr>
<td>Swelling in legs</td>
<td>0.34</td>
<td>42</td>
<td>92</td>
<td>71</td>
<td>77</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>0.42</td>
<td>52</td>
<td>91</td>
<td>69</td>
<td>83</td>
</tr>
</tbody>
</table>

Weisbord SD et al. CJASN 2007; 960-67
Treatment of pain in HD

- Evaluation of pain tx in 205 Canadian HD pts
- Brief Pain Inventory and McGill Pain Questionnaire to assess presence of pain
- Pain Management Index to assess tx

Davison SN - AJKD 2003; 1239-47
Treatment of pain in 205 Canadian HD pts

• 50% reported pain
• 55% of these pts reported severe pain
• 35% with pain receiving no therapy
• 75% on analgesics reported tx to be ineffective

Davison SN- AJKD 2003;1239-47
Renal providers largely unaware of sx in HD pts

Tx of pain is sub-optimal

Relevance to our pt:
- His sx – pain, sexual dysfunction, sleep disturbance are likely to remain un-assessed by renal provider and untreated
Symptom assessment instruments in ESRD

• **Dialysis Symptom Index**
  – 30-item questionnaire assesses presence and severity of sx
  – Validated in HD patients

• **Edmonton Symptom Assessment Scale**
  – 9-item tool that assesses symptom distress
  – Modified for ESRD to include 10th item – pruritis
  – Validated in the dialysis population
Pain in patients with ESRD

• Found to be present in ~ 50% of pts
• Under-assessed
• Under-treated
• Associated with:
  – Depression
  – Insomnia
  – Consideration of withdrawal of dialysis
Efficacy of Pain Tx

Barakzoy AS and Moss AH. JASN 2006;17:3198-3203
Medications to avoid in ESRD

- Morphine
- Meperidine
- Codeine
- Propoxyphene
Medications with important dose limitations

- **Tramadol** – peripherally/centrally acting non-narcotic
  - Avoid with concomitant SSRI
  - Max dose 50 mg bid

- **Gabapentin**
  - Off label use for pain
  - Max dose 300 mg qd (supplemental dose after HD)
  - Somnolence is primary side effect

- **Acetaminophen**
  - Max total dose 4g daily → hepatotoxicity

- **Tri-cyclic anti-depressants** – ↑ risk of side effects in ESRD – dose limitations
Nociceptive pain algorithm

**STEP ONE**

Acetaminophen +/- non-pharmacologic adjuvants

**STEP TWO**

Acetaminophen +/- non-pharmacologic adjuvants
NSAIDS if no contra-indication and no residual GFR

**STEP THREE**

Hydromorphone 1 mg po q4-6h + 1 mg prn for breakthrough pain
Fentanyl 0.25-1.0 mcg/kg
Titrate up slowly until analgesic effect or intolerable side effect

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Fentanyl 0.25-1.0 mcg/kg
Titrate up slowly until analgesic effect or intolerable side effect

Hydrocodone 5 mg po q4h prn; Oxycodone 5 mg po q4h prn;
tramadol 25 mg po qd (max dose 50 mg bid)
+/- non-opioid analgesics/adjuvants
Neuropathic pain algorithm

**Desipramine**
- 10 mg PO QHS - Titrate to adequate pain control or max dose of 150mg PO QHS
  * If pain control inadequate, institute Nociceptive Pain Algorithm

**STEP THREE**
- **Pregabalin**
  - Start 25 mg PO qd with 1 supplement dose of 25mg or 50mg after dialysis treatment
  - If ineffective after 2-4 wks, titrate off over one wk and start Desipramine

**STEP TWO**
- **Gabapentin**
  - Start 100 mg QHS and weekly by 100 mg per night to a max dose of 300 mg QHS
  - If ineffective at max tolerated dose, d/c and start Pregabalin

**STEP ONE**
Additional sx – erectile dysfunction

• Found in 82% of male HD pts in one study
• 42% of these pts reported ED to be severe
• ED associated with ↓ aspects of HRQoL
• A number of studies have shown that sildenafil (phosphodiesterase-5 inhibitor) is effective for ED in HD pts and is associated with improved HRQoL

Additional sx - depression

- Depression present in ~ 25-30% of HD pts
- Multiple studies showing depression associated with ↓ HRQoL
- Growing # studies showing depression associated with ↑ mortality
- Small studies demonstrate certain anti-depressant medications efficacious in HD pts
- Paucity of good data on tx of depression

Patient’s original question to me was:

- Are you going to maintain my Kt/V > 1.2 consistently?
- Will my hematocrit be maintained between 33-36%?
- What is the target iPPTH when I start HD?
- How am I going to feel on hemodialysis?
Unfortunately, my answer could have been....

You’ll likely have lots of bothersome sx that may contribute to lower quality of life and which may not be fully assessed or treated
Conclusions & future directions

• Sx common, severe $\rightarrow$ impaired pt well-being
• We under-assess and under-tx sx in HD pts
• Strategies to improve sx assessment & tx are needed
• Sx alleviation may be 10 means of improving HRQoL and patient-centered outcomes in this population