Depression, Anxiety, and Burnout in Peritoneal Dialysis

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Disclosures

• Financial Conflict of Interest:
  • Member, Scientific Advisory Board: Zytoprotec
  • Member, Board of Trustees, Northwest Kidney Centers

Goals of My Presentation

Depression

Anxiety

Liberally borrow from work done with hemodialysis patients to make my points to overcome limitations of data specifically in those undergoing PD
Depression is Common in PD Patients

One in every three patients undergoing PD has significant depressive symptoms.

In dialysis patients, depression often sub-clinical

<table>
<thead>
<tr>
<th>Depression Indicator</th>
<th>Prevalence of Depression</th>
<th>Depression Index</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Europe</td>
<td>United States</td>
</tr>
<tr>
<td>Physician-diagnosed, by medical record</td>
<td>16.2</td>
<td>19.0</td>
</tr>
<tr>
<td>Self-Reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;Downhearted and blue&quot;</td>
<td>24.8</td>
<td>22.6</td>
</tr>
<tr>
<td>&quot;So down in the dumps&quot;</td>
<td>16.6</td>
<td>16.6</td>
</tr>
</tbody>
</table>

Patients:
- Hesitation to bring up their emotional experiences at a doctors' visit for "physical" problems
- Perception that this is a "phase" they will pull through
- "Stigma" or perception they are not strong enough

Physicians:
- Lack of skill or expertise to suspect and diagnose depression

Kidney Failure Puts a Lot of Demands on Patients

- PD has many advantages but it still needs to be done every day
- Many therapy innovations require patients to do more and not less
- Numerous restrictions on diet of a PD patient:
  - Low salt and phosphorus, high protein
- Very high pill burden (median, 19 per day)
- Numerous care transitions – from hospital to home or others
- Depression makes it harder for patients to do everything right all the time
Depression and Cognitive Function

458 PD patients from five units in China:
- Depression assessed using Zung self-rating depression scale
- Cognitive function using modified Mini-Mental Scale

Patients with mild or moderate/severe depression had a higher prevalence of:
- Overall cognitive impairment
- Executive dysfunction
- Impaired immediate or delayed memory

Patients with Depression have Lower Adherence

<table>
<thead>
<tr>
<th>Study Population</th>
<th>Studies</th>
<th>Median r</th>
<th>Mean weighted r</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESRD</td>
<td>6</td>
<td>-0.34</td>
<td>-0.32</td>
<td>3.44</td>
</tr>
<tr>
<td>Non-ESRD</td>
<td>6</td>
<td>-0.24</td>
<td>-0.21</td>
<td>2.77</td>
</tr>
</tbody>
</table>

DiMatteo et al, Arch Intern Med 2000; 160: 2101-7

Depressive Symptoms and HD Adherence

For every 5-point higher PHQ-9 score, adjusted incident rate ratio for:
- Missed HD: 1.21 (1.10, 1.33)
- Abbreviated HD: 1.08 (0.83, 1.40)

Depression and Peritonitis

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Risk Ratio</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDI ≥ 11</td>
<td>2.7</td>
<td>1.34-6.08</td>
</tr>
<tr>
<td>Age ≥ 65 y</td>
<td>0.8</td>
<td>0.29-1.48</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1.0</td>
<td>0.46-2.17</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>0.6</td>
<td>0.39-1.79</td>
</tr>
<tr>
<td>Race</td>
<td>0.9</td>
<td>0.39-2.35</td>
</tr>
</tbody>
</table>

625 patients assessed using Beck Depression Inventory

Recap
One in three PD patients have significant depressive symptoms
The symptoms are sub-clinical and not easily diagnosed in routine care
But these sub-clinical symptoms are enough to amplify the health problems of PD patients:
- Decreased adherence
- Higher ED visits and hospitalizations
- Higher risk for peritonitis

Diagnosis of Depression
Major depressive disorder is a psychiatric diagnosis that requires a structured clinical interview:
- Requires patients to meet 5 of the 9 criteria for a correct diagnosis

Overview of diagnostic issues
- Depressed mood or loss of interest or pleasure in daily activities for more than two weeks
- Mood represents a change from a person's baseline
- Impaired function: social, occupational, educational

We nephrologists are not trained to do these interviews
Diagnosis of Depression

Administer a **screening instrument**:
- Patient Health Questionnaire-2 (PHQ-2)
- Patient Health Questionnaire-9 (PHQ-9)
- Beck Depression Inventory-Ⅱ (BDI)
- Center for Epidemiologic Studies Depression Scale (CESD)
- Hamilton Depression Rating Scale (HDRS)
- Hospital Anxiety and Depression Scale (HADS)
- Major Depression Inventory (MDI)
- Quick Inventory of Depressive Symptoms (QIDS)
- Geriatric Depression Scale (GDS)

Remember – these are screening instruments for depressive symptoms and **they DO NOT make a diagnosis of major depressive disorder**

And Cut-Off Scores for Some Screening Instruments Are Different in CKD/ESRD

<table>
<thead>
<tr>
<th>Scale</th>
<th>No. of Items</th>
<th>Score Range</th>
<th>Usual Cut-Off</th>
<th>Cut-Off in CKD (Sens, Spec)</th>
<th>Cut-Off in ESRD (Sens, Spec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDI</td>
<td>9</td>
<td>0‐63</td>
<td>≥ 10</td>
<td>≥ 12 (89%, 88%)</td>
<td>≥ 14‐16 (62‐91%, 81‐85%)</td>
</tr>
<tr>
<td>QIDS‐SR</td>
<td>16</td>
<td>0‐27</td>
<td>≥ 10</td>
<td>≥ 10 (91%, 88%)</td>
<td>≥ 10 (81%, 83%)</td>
</tr>
<tr>
<td>CESD</td>
<td>20</td>
<td>0‐60</td>
<td>≥ 16</td>
<td>≥ 18 (89%, 83%)</td>
<td></td>
</tr>
<tr>
<td>PHQ</td>
<td>9</td>
<td>0‐27</td>
<td>≥ 10</td>
<td>≥ 10 (92%, 92%)</td>
<td></td>
</tr>
</tbody>
</table>


Significant overlap between symptoms of depression with those experienced by patients with kidney diseases – either from uremia or side-effects of medications

Screening for Depression

**PHQ-2**
PHQ-2
Psychometric Properties (Gen Pop)

<table>
<thead>
<tr>
<th>Prevalence, 7%</th>
<th>Prevalence, 14%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sens Spec PPV</td>
<td>Sens Spec PPV</td>
</tr>
<tr>
<td>1</td>
<td>97.6 59.2 15.4</td>
</tr>
<tr>
<td>2</td>
<td>92.7 73.7 21.1</td>
</tr>
<tr>
<td>3</td>
<td>82.9 50.0 38.4</td>
</tr>
<tr>
<td>4</td>
<td>73.2 93.3 45.5</td>
</tr>
<tr>
<td>5</td>
<td>53.7 96.8 56.4</td>
</tr>
<tr>
<td>6</td>
<td>26.8 99.4 78.6</td>
</tr>
</tbody>
</table>

No data for patients with ESRD

Kroenke et al, Med Care 2003

Treatment Options for Depression

Pharmacologic Therapy
- Selective Serotonin Receptor Uptake Inhibitors (SSRIs)
- Serotonin Norepinephrine Reuptake Inhibitors

Psychotherapy
- Acceptance and Commitment Therapy; Cognitive Therapy; Cognitive Behavioral Therapy; Interpersonal Therapy; Psychodynamic Therapy

Complementary and Alternative Medicine
- Acupuncture; meditation; ω-3 fatty acids; S-adenosyl-L-methionine; St. John’s wort; yoga

Exercise

Limited Data on Treatment in ESRD
Group CBT

90 HD patients at two dialysis facilities randomized to group CBT or usual care
Re-evaluation at 3 months, 85; at 9 months, 74

Improved perception of duration of kidney disease, quality of social interaction, sleep, and mental component summary of health-related quality of life

Duarte et al, Kidney Int 2009; 76: 414-21
Limited Data on Efficacy of Treatment

Individual CBT

65 HD patients at two dialysis units randomized to immediate individual CBT in dialysis facility and wait-list for treatment; 55 completed the intervention


Limited Data on Efficacy of Treatment

Drug Therapy

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Drug</th>
<th>N</th>
<th>Depression Scale</th>
<th>Key Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blumenfield, '97</td>
<td>Fluoxetine</td>
<td>14</td>
<td>Ham-D and others</td>
<td>No significant difference between fluoxetine and placebo</td>
</tr>
<tr>
<td>Yazici, '12</td>
<td>Escitalopram</td>
<td>62</td>
<td>DSM-IV</td>
<td>Significantly lower depression scores compared with placebo</td>
</tr>
<tr>
<td>Taraz, '13</td>
<td>Sertraline</td>
<td>50</td>
<td>BDI-II</td>
<td>Significantly greater improvement with sertraline than placebo</td>
</tr>
<tr>
<td>Friedli, '17</td>
<td>Sertraline</td>
<td>30</td>
<td>BDI-II and others</td>
<td>Scores improved with both sertraline and placebo; no difference between the two groups</td>
</tr>
</tbody>
</table>

Yazici et al, Klinik Psikofarmakoloji Bulteni 2012; 23-30
Taraz et al, Int Immunopharmacol 2013; 17: 917-923

Comparative Efficacy of CBT and Drugs

ASCEND

*Multi-center randomized controlled trial in patients undergoing in-center hemodialysis primarily to compare the efficacy of 12-week treatment with CBT and anti-depressant drug therapy

* Conducted in three metropolitan areas – Albuquerque, Dallas, and Seattle – in 41 different dialysis units:
  - In Seattle, we enrolled patients from NKC, PSKC, ONC, and DVLSD

* Approached 2857 patients undergoing hemodialysis for at least three months and asked them to complete a screening instrument for depression, BDI-II; 2468 (90%) agreed and 120 randomized to treatment

ASCEND

CBT was conducted in the dialysis unit by a therapist while the patient was undergoing hemodialysis:
- Patients were given the choice to do it outside the dialysis unit, but few selected that choice

Drug therapy was started at a low dose and changes in dose were made based upon periodic assessment of depressive symptoms and side-effects of drugs using “Measurement Based Care”

Results

- Depression scores decreased with both treatments
- At least 50% decrease in scores:
  - CBT: 50% (95% CI, 24%, 69%)
  - Sertraline: 47% (95% CI, 35%, 59%)
- Remission:
  - CBT: 39% (95% CI, 27%, 52%)
  - Sertraline: 40% (27%, 52%)

Serious adverse event rate similar; other adverse events more frequent with sertraline

Other Lessons

- Many people who have high scores on screening instruments do not have depression and don’t need treatment
- A lot of people are treated for depression but do not get enough medications in doses high enough for them to work.
- A lot of people feel there is a stigma with the diagnosis of depression and do not like to be given the label of depression
- Both medicines and CBT work similarly with medications slightly better but with more side effects
- Patients should be treated based on what is available, how much it may cost a patient, and what they prefer
Recap

Depression is sub-clinical and not readily diagnosed in routine care.

Best to use any one of the screening instruments:
- In US, PHQ-2 is being used and administered once yearly.

Discuss with patients the next steps within scope of what is feasible:
- Refer to psychiatrist.
- Offer a trial of anti-depressant drug.
- Offer a trial of cognitive behavioral therapy.

At this time, we do not know if a strategy of routine screening for depression results in better health outcomes for patients.
- But seems reasonable as long as there are well-thought plans in place for management of patients.

Anxiety in ESRD

More Common than Depression?

<table>
<thead>
<tr>
<th>N</th>
<th>Instrument</th>
<th>Point Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>127</td>
<td>Self-Rating Anxiety Scale</td>
<td>Symptomatic: 33%</td>
</tr>
<tr>
<td>40</td>
<td>Hospital Anxiety and Depression Scale</td>
<td>Anxiety Disorder: 30%</td>
</tr>
<tr>
<td>70</td>
<td>Hospital Anxiety and Depression Scale</td>
<td>DSM-IV Anxiety Disorder, 46%</td>
</tr>
<tr>
<td>175</td>
<td>Beck Anxiety Inventory</td>
<td>53% (28% moderate-severe)</td>
</tr>
</tbody>
</table>

In patients undergoing PD, associated with higher technique failure (Grius et al, 2016).

Many Traumatic Experiences

Many Related to or From Need for Dialysis.
Aftermath of Hurricane Katrina

- 41% No PTSD or depression
- 29% PTSD +/Depression -
- 10% PTSD -/Depression +
- 10% PTSD +/Depression +

391 HD patients at 9 facilities in New Orleans; phone interview 9-15 months later


Summary and Conclusions

Depression:
- Is common
- Has broad effects on patients’ health and well-being
- Is challenging to diagnose
- But is treatable

Anxiety:
- Is common but
- Much less well studied and
- Treatment approaches uncertain

Questions?