

PSYCHIATRIC CONSULTATION IN RENAL DISEASE

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Disclosure Statement

- Dr. Hemlata Joshi

- With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company in the past 24 months which could be considered conflict of interest.

Objectives

- 1. To learn about the most prevalent psychiatric disorders in ESRD
- 2. To have better understanding of cognitive impairment in ESRD patients
- 3. To learn about the management of these psychiatric disorders

The ESRD Population

- 80,000 new cases of ESRD each year
- More than 340,000 treated for kidney failure in 2002
- 240,000 receiving maintenance dialysis
- 100,000 functioning kidney transplant
- Number of patients starting renal replacement therapy increases by 5-7% each year

Causes of ESRD

- Diabetes – 1/2 of all ESRD incident cases
- Hypertension
- Generalized arteriosclerosis
- Lupus
- AIDS
- Primary renal disease

Psychiatric Pathology in ESRD

- Depression
- Anxiety
- Delirium
- Cognitive impairment
- Sleep disorders
 - RLS
 - PLMD
 - Insomnia

Depression

- Higher in renal failure than in ischemic heart disease and cerebrovascular disease
- Hospitalization with psychiatric disorders 1.5 to 3 times higher for hemodialysis patients

DSM IV TR Dx for Depression

- A. Five (or more) of the following symptoms during the same 2-week period
- At least one of the symptoms is:
 - depressed mood or
 - loss of interest or pleasure
- **Note:** Do not include symptoms clearly due to a general medical condition

DSM IV-TR Dx Cont.

- 1. Depressed mood
- 2. Markedly diminished interest or pleasure
- 3. Significant weight loss or gain or decrease or increase in appetite

DSM IV-TR Dx Cont.

- 4. Insomnia or hypersomnia
- 5. Psychomotor agitation or retardation
- 6. Fatigue or loss of energy

DSM IV-TR Cont.

- 7. Feelings of worthlessness or excessive or inappropriate guilt (not merely self-reproach or guilt about being sick)
- 8. Diminished ability to think or concentrate, or indecisiveness
- 9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation

Difficulties with Diagnosis

- Many symptoms of medical illness resemble depression
- Patients often have wishes for death with advanced medical disease in absence of depression
- Multiple physical symptoms reduce pleasure and interest
- Amplified somatic symptoms, non compliance or refusal with treatment could be due to depression

Differentiating between ESRD and Depression

- Symptom severity is disproportionate to the degree of illness and physical disability
- Symptoms persist without attenuation with no real perpetuating factor

Differentiating between ESRD and Depression

- Non neuro-vegetative symptoms:
 - depressed mood
 - loss of interest
 - suicidal ideation
 - excessive guilt
 - excessive despondency and discouragement

Screening Tools

- Beck Depression Inventory (BDI)
- Patient Health Questionnaire (PHQ-9)
- BDI >14-16
- PHQ-9 > 10

Treatment of Depression

- Selective Serotonin Reuptake Inhibitors widely prescribed in ESRD
- Only 2 small short term randomized controlled studies have shown some benefit of paroxetine and fluoxetine
- No reported controlled clinical trials of psychotherapy for depression in renal patients
- Cognitive Behavioral Psychotherapy (CBT) maybe an effective intervention strategy

Anxiety

- General or specific to the dialysis process
- General anxiety:
 - dramatic life change
 - uncertainty about future
 - ability to cope with the demands of dialysis and expectations of staff and family
 - imminent mortality

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Anxiety

- Specific anxiety:
 - Rapid removal of fluid and electrolytes may produce hypotension, muscle cramping, nausea and vomiting that can exacerbate a panic attack or worsen anxiety symptoms
 - Needling often causes an inordinate degree of anxiety for both the patient and nurse

Anxiety

■ PTSD

- re-traumatized during each dialysis treatment
- previous issues of loss of control from physical or sexual abuse
- repeatedly poked, prodded
- no escape for 4 hour period

Anxiety

- Fears of Mortality
- Annual mortality rate of 23%
- Expected remaining lifetime of a dialysis patient $\frac{1}{4}$ of age and sex matched general population.

Cognitive Disorders

- Delirium
- Stroke
- Cognitive Impairment

Delirium

- Common in ESDR population
- Can be caused by:
 - uremia
 - electrolyte disturbances
 - severe malnutrition
 - impaired metabolism
 - cerebrovascular disease
 - adverse treatment effects

Delirium

- Can be improved by:
 - intensifying dialysis
 - parathyroidectomy
 - improved control of diabetes mellitus

Disequilibrium Syndrome

- Progressive cognitive impairment approaching dialysis day
- After dialysis brief period of delirium lasting minutes to hours
- Rapid changes in fluid and electrolytes during the dialysis session

Cognitive Impairment (CI)

- Increased CI caused by higher rates of:
 - stroke
 - TIA
 - advanced age
 - Hemodialysis itself
 - ESRD
- Neuro-imaging has shown increased:
 - prevalence of silent cerebral white matter lesions
 - periventricular hyper intensities on MRI
 - greater degree of brain atrophy
- Changes related to length of time on Hemodialysis

Cognitive Impairment

- Develops in patients with chronic renal disease prior to the development of ESRD
- Weiner et al. showed that patients with GFR of less than 45 were 2.5 times more likely to develop CI than those with a GFR greater than 60

Cognitive Impairment

- Murray et al. found:
 - < than 15% had normal cognition
 - > 1/3 severe cognitive impairment
 - > 1/3 moderate cognitive impairment
- HD patients 3.5 x severe CI compared with controls after adjusting for demographic variables, vascular risk factors and vascular disease

Question to be researched further

- How much of the cognitive impairment observed in hemodialysis patients is due to?
 - the dialysis process itself
 - uremia
 - and/or the metabolic processes associated with renal failure
 - some combination of all of the above

Mechanism of CI by Dialysis

- Dialysis may induce cerebral ischemia by:
 - acute intravascular volume loss and fluid shifts that induce cerebral edema, decrease intracerebral blood pressure, blood velocity and cerebral perfusion
- Higher dialysis dosing may make this phenomenon worse

Renal Psychopharmacology The Basics

- Fat soluble
- Large volumes of distribution
- Metabolized in the liver
- Metabolites eliminated in the urine and bile

Renal Psychopharmacology The Basics

- Majority of these drugs safe in ESRD
- Special attention to:
 - active metabolites
 - parent drug/ metabolite highly protein bound
 - altered pharmacokinetics and pharmacodynamics

Renal Psychopharmacology The Basics

- Exception:

- | | |
|------------------|-------------|
| – Lithium | Gabapentin |
| – Topiramate | Venlafaxine |
| – Desvenlafaxine | Bupropion |
| – Memantine | Risperidone |
| – Paliperidone | Paroxetine |

Renal Psychopharmacology The Basics

- Most psychotropics - not dialyzable
 - lipophilicity
 - large volumes of distribution
- Dosing guidelines based on CrCl not available
- 2/3 rule

QTc Prolongation

- Electrolyte disturbances ↑ renal failure
- TCAs
- Lithium
- Typical & atypical antipsychotics
- Monitor regularly

Pharmacotherapy of Anxiety and Depression

- SSRIs
 - Bupropion
 - Buspirone
 - Risperidone
 - Paliperidone
 - Benzodiazepines
- SNRIs
Mirtazapine
TCAs

SSRIs

- Fluoxetine
- Sertraline
- Citalopram
- Paroxetine/Paroxetine CR

Fluoxetine

- Best studied in ESRD
- Efficacious and non toxic
- Renal function does not alter levels of fluoxetine or norfluoxetine

Sertraline and Citalopram

- Similar kinetics
- Minimally changed in ESRD
- Normal dosing can be used

Paroxetine

- Plasma concentrations increased in renal impairment
 - Mild RI – no dose change
 - Mod RI- 50-70% of usual dose
 - Severe RI – 10mg/day
 - ↑10mg/week
 - max dose 40mg

Paroxetine CR

- 12.5mg
- ↑ 12.5mg/week
- Max dose 50mg/day

SNRI

- **Venlafaxine**
 - Metabolites eliminated in urine
 - Regular monitoring of blood pressure recommended
 - Mild-mod RI – 75% of dose
 - Severe RI 50% of dose
 - HD – 50% of dose. Dose after dialysis session

SNRI

■ Desvenlafaxine

- 45% excreted unchanged
- Mild RI – no dose change
- Mod RI – no greater than 50mg/day
- Severe RI – 50mg every other day

Bupropion

- Active metabolites excreted by kidney
- Metabolites accumulate in dialysis
- Predispose to seizures
- Reduce initial dose

Mirtazapine

- Mod RI – clearance decreased by 30%
- Severe RI clearance reduced by 50%

Buspirone

- Considerable inter-individual variability in kinetics
- Benefit from 25% - 50% dose reduction
- Not recommended in severe RI

TCA's

- Cleared and metabolized by the liver
- Can be dosed normally
- All the issues of toxic effects apply
- Not be used first line
- Low dosing effective for neuropathic pain, urticaria and insomnia

Atypical Agents

- Aripiprazole, quetiapine, olanzapine, clozapine – no dose adjustment
- Ziprasidone – no recommendations

Risperidone

- Clearance decreased in RI
- Initiate therapy at 0.25-0.5mg bid
- Increases > than 1.5mg made at 7 days intervals

Benzodiazepines

- Metabolized in the liver
- Dose reduction is generally not necessary
- Caution with midazolam, chlordiazepoxide as highly protein bound
- Normal doses of diazepam, alprazolam and clonazepam
- Lorazepam prolonged half life
- Caution with dosing and frequency

Dialyzable Psychotropic Drugs

Medication	Conventional Hemodialysis	High-Permeability Dialysis	Peritoneal Dialysis
Carbamazepine		Yes	
Gabapentin	Yes	Likely	
Lamotrigine		Clearance increased by 20%	
Lithium	Yes	Yes	Yes
Pregabalin	Yes	Likely	
Topiramate	Yes	Likely	
Valproate	Yes	Likely	

Palliative Care

- Withholding or withdrawing renal replacement therapy
- Decision to not start dialysis more common than withdrawal
- Encephalopathic and lack sufficient decision making capacity
- Seek TSDM to provide involuntary dialysis until patient's mental status improved enough to make an informed decision

Palliative Care

- Withdrawal dialysis is often appropriate for the dying dialysis patient
- Provides quick death
- Mean time to death after stopping dialysis 8 days
- Dialysis termination does not cause pain or discomfort
- Lethargy leading to coma and death

Withdrawing Dialysis

- Patients with severe and irreversible dementia
- Patients who are permanently unconscious (i.e. a persistent vegetative state)
- Patients with end stage cancer or end stage lung, liver or heart disease who need considerable assistance with activities of daily living and may be confined to bed, chair, or involved in a hospice program
- Patients with severe mental disability, who are uncooperative with the procedure of dialysis itself, are unable to interact with the environment or other people or are persistently combative with family or staff

Withdrawing Dialysis

- Patients with severe, continued and unrelenting pain in whom dialysis may prolong life for a short period of time but will also prolong suffering
- Hospitalized patients (especially elderly) with multiple organ system failure that persists after 3 days of intensive therapy

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