Managing behavioral health needs of patients with dementia

Gail Li, MD, PhD

Associate Professor

Dept. of Psychiatry and Behavioral Sciences

UW School of Medicine

&

VA Puget Sound Health Care System

June 2, 2021

Dementia

- Clinical syndrome
- Multiple cognitive deficits
- Decline and functional impairment

Alzheimer's disease (AD)

Vascular dementia (VaD)

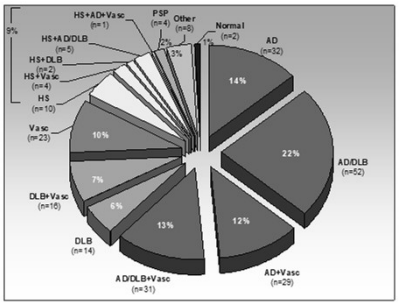
Dementia with Lewy bodies (DLB)

Multiple etiologies

Other neurodegenerative disorders (e.g., frontotemporal lobe dementia, Parkinson's disease, and Huntington's disease)

Other etiologies (e.g., HIV, general medical conditions, substance-induced persisting dementia)

Neuropathological diagnosis in 233 community-based dementia cases



Courtesy of Dr. Tsuang

Different issues at different stages

- **Early stage: Patient may function independently**
  - » Memory and executive function impairments
  - » Important to provide education, support and companionship, and to help plan for the future
  - » Driving issues

Different issues at different stages

- **Middle stage - moderate**
  - » May last many years
  - » Requires a greater level of care
  - » Patient needs to stop driving
  - » Language and behaviors issues
    - ♦ Depression, anxiety, irritability, and repetitive behaviors
    - ♦ Sleep changes, physical and verbal outbursts, and wandering

Different issues at different stages

- **Late stage**
  - » Difficulties in eating and swallowing
  - » Patient needs assistance walking and eventually is unable to walk
  - » Vulnerable to infections, especially pneumonia
  - » Loses the ability to communicate with words

Common behavioral disturbances in patients with dementia

- Depression and anxiety
- Sleep-wake disturbances
- Disruptive behaviors

Depression and anxiety

- Important to differentiate depression from apathy
- Treatment
  - » Behavioral activation and sleep hygiene
  - » Antidepressants are effective for depressive symptoms and increased irritability
  - » Start low, go slow but go!

Examples of antidepressants in geriatric patients

	Usual dose (mg/d)	Starting dose (mg)	Pros and Cons
Citalopram	20 – 40	10 qd	Well tolerated, ↑ QTc
Sertraline	50 – 150	25 qam	Non-sedating, GI side effect
Paroxetine	10 – 30	10 qhs	Sedating and anticholinergic
Fluoxetine	20 – 60	10 qam	Activating, long half-life, drug interactions
Venlafaxine	150 – 225	25 or 37.5 qam	Good for melancholic depression. ↑ BP
Mirtazapine	15 – 30	7.5 qhs	↑ Appetite and sedation
Duloxetine	20 - 60	10 qhs	Good for neuropathic pain

Sleep-wake disturbances in dementia

- Normal aging related changes in sleep:
  - » ↓ total sleep time, becomes lighter and more fragmented
  - » Phase advancement
- Common sleep disorders
  - » Irregular sleep-wake rhythm disorder
  - » Restless legs syndrome
  - » Rapid eye movement sleep behavior disorder (RBD) is a parasomnia caused by loss of muscle atonia during REM sleep, which results in patients "acting out" their dreams. Common in PD and DLB
  - » Sleep apnea
  - » Insomnia

Assessment of sleep disturbances

- Difficulty falling asleep or staying asleep
- Excessive daytime sleepiness
- Unusual sleep-related behaviors or movements
- Sleep habit and environment
- Comorbid conditions, and medications that may disrupt or alter sleep patterns

Management of sleep disturbances

- **Nonpharmacologic interventions**
  - » Individualized according to patient and caregiver needs
  - » Management of polypharmacy
  - » Consistent sleep-wake schedules
  - » Sleep hygiene and environment
  - » Light therapy, 30 min qam, 10,000 Lux with full spectrum

Management of sleep disturbances

- **Pharmacotherapy, less role in management**
  - » Limit benzodiazepine use and avoid Zolpidem
  - » Melatonin
  - » Trazodone

Disruptive behaviors

- Irritable and anger outbursts
- Agitation or aggression
- Uncooperativeness with necessary care
- Pressured pacing and restlessness
- Hallucination and delusions

Assessment of disruptive behaviors

- Assess risk of harm to self or others
- Implement safety measures
  - » Elevated level of care, or one-on-one supervision
  - » Hospitalization if necessary
  - » Provide caregiver supports
- Identify and treat underlying medical conditions
- Consider short-term drug therapy if at high risk of harm to self or others

Underlying causes

- Delirium (UTI, or other infections)
- Pain
- Medications
  - » New meds, drug-drug interaction
  - » Opioids, benzodiazepine, and anticholinergic
- Depression and anxiety
- Sleep disturbances
- Sensory deficits (hearing and vision)

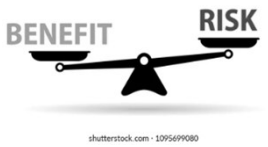
Non-Pharmacotherapy

- » Identifying the symptom and understanding its cause
- » Identifying triggers:
  - ♦ New caregivers
  - ♦ Admission to a hospital
  - ♦ Presence of houseguests
  - ♦ Being asked to bathe or change clothes
- » Routine activity
- » Caregiver education:
  - ♦ Don't disagree, respect the person's thoughts even if incorrect
  - ♦ Redirect the person to participate in an enjoyable activity or offer comfort food

Pharmacotherapy for disruptive behaviors

- Alpha-1 adrenoreceptor antagonist, prazosin
- Antipsychotics, mainly atypical antipsychotics for psychosis and severe disruptive behaviors
  - » Concern of sedation and increased mortality
  - » Short-term use, and consider to stop when it is not needed
- Mood stabilizers - such as valproic acid
  - » benefit uncertain

Risk vs benefit of pharmacotherapy



Impact of the behavior disturbances

- Reflects suffering on the part of patients
- Causes severe stress in both home and institutional caregivers
- Interferes with providing basic care
- Can pose a threat of harm to self and others
  - » Nighttime wandering and fall
- Contributes to functional disability
- Increases rate of decline and death

Prazosin

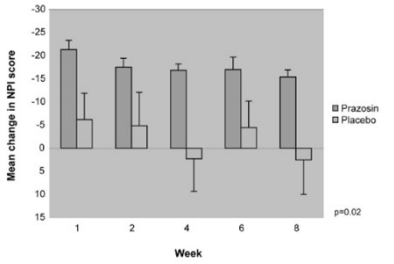
- The noradrenergic system is the brain “adrenaline” system for attention and arousal
- Excessive noradrenergic activity contribute to agitation in AD
- Prazosin is a centrally acting generic alpha-1 adrenoreceptor antagonist
- Prazosin has been used for decades to treat hypertension and benign prostatic hypertrophy urinary symptoms with good safety profile
- It is “off label” use for disruptive behaviors currently

Pilot Study of Prazosin for Disruptive Agitation in AD Dementia

- 22 patients with AD dementia and frequent disruptive agitation (mean age 81 ± 11 years).
- Randomized to prazosin (n=11) or placebo (n=11) for 8 weeks.
- Prazosin was started with 1mg qhs and increased by increments of 1 to 2 mg every 3 to 7 days up to a maximum of 2mg qam and 4mg qhs (mean achieved dose 5.7 ± 0.9 mg/day).
- Primary outcome measures: NPI, BPRS CGIC.

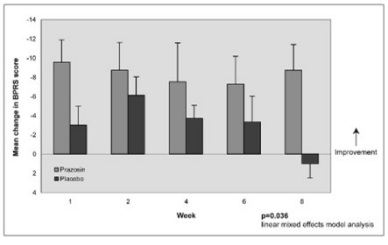
Wang et al. Am J Geriatr Psychiatry. 2009, 17:744-51

Pilot Study of Prazosin for Disruptive Agitation in AD Dementia: Neuropsychiatric Inventory (NPI)



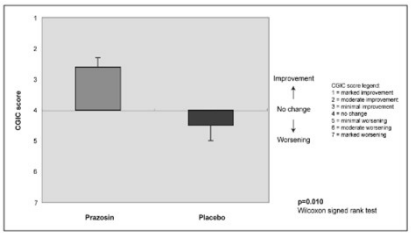
Wang et al. Am J Geriatr Psychiatry. 2009, 17:744-51

Pilot Study of Prazosin for Disruptive Agitation in AD Dementia: Brief Psychiatric Rating Scale (BPRS)



Wang et al. Am J Geriatr Psychiatry. 2009, 17:744-51

Pilot Study of Prazosin for Disruptive Agitation in AD Dementia: Clinical Global Impression of Change (CGIC)



Adverse Events Were Similar for Prazosin and Placebo Groups

Number of Occurrences of Adverse Events

	Prazosin group	Placebo group	Both groups combined
Sedation	3	3	6
Confusion	2	4	6
Hypotension	2	1	3
Dizziness on Standing	1	0	1

Prazosin for Disruptive Agitation in Alzheimer's Disease: PEACE-AD

- Phase IIb multicenter, double-blind, placebo-controlled RCT for disruptive agitation in long-term care and home dwelling participants
- Funded by NIA via the Alzheimer's Disease Cooperative Study with supplement from Alzheimer's Association
- 15 sites across US
  - » Some sites home dwelling participants only
  - » Some sites home dwelling plus long-term care

peaceAD
prazosin for disruptive agitation in Alzheimer's disease

Curtesy of Dr. Elaine Peskind

Prazosin

- Starting dose: 1mg qhs
- Increasing by 1mg every 3-7 days as tolerated
- Target dosage: 2-6 mg/day in divided doses
- Consider dosing in afternoon to prevent sundowning agitation
- Adverse effects
  - » Orthostatic hypotension, dizziness on standing
  - » 1st dose effect
  - » Slightly sedation in some patients

Examples of atypical antipsychotic medication usage in geriatric patients

	Usual dose	Starting dose and titration	Pros and Cons
Quetiapine	25 – 200mg	12.5mg qhs, ↑ 12.5mg q3-7 days	More sedating
Olanzapine	5 – 10mg	2.5mg qhs, ↑ 2.5mg q3-7 days	Sedating
Risperidone	1 – 2mg	0.25mg qhs, 0.25mg q3-7 days	Higher risk of EPS

Management of DLB

- Dopaminergic therapies and anticholinergic medications can adversely affect cognition/behavior, leading to confusion and psychosis
- ChEIs (Rivastigmine and Donepezil) improve cognition and functions
- Efficacy of memantine is less clear but well-tolerated and may have benefit
- Avoid antipsychotics; if needed, may use low dose quetiapine for visual hallucinations and delusion
- ChEIs may reduce apathy, hallucinations, and delusions

Pimavanserian (Nuplazid)

- An 5HT2A receptor inverse agonist
- Only FDA approved drug for the tx of psychosis in PD
- **34 mg qd without titration**
- Switching from an antipsychotic with high risk of motor side effects (ie, haloperidol, risperidone): Stop the antipsychotic ASAP and start pimavanserin after washout; motor worsening may persist for 30 days
- Switching from quetiapine: Add pimavanserin 34 mg/day to quetiapine for 4 wks and then begin to reduce quetiapine by 25% weekly until reaching 12.5 mg, then d/c

Summary

- Non-pharmacotherapy is extremely important for management of behavioral disturbances
- Assessing risk and benefit of pharmacotherapy
- Pharmacotherapy
  - » Antidepressants for depression, anxiety and increased irritability
  - » Prazosin (α1 blocker) for disruptive behaviors
  - » Atypical antipsychotics for psychosis and severe disruptive behaviors

A case study