BEST PRACTICES: MEDICATION MANAGEMENT FOR THE BEHAVIORAL SYMPTOMS OF DEMENTIA

Jennifer Serafin, GNP-BC, GS-C

OBJECTIVES

- Summarize how to use the NPI-Q tool, especially when evaluating the effectiveness of medication treatments.
- Name 2 medications that can negatively impact Persons with Dementia (PWD), leading to increased Dementia Behaviors.
- Describe the classes of medications used to treat Behavioral and Psychological Symptoms of Dementia (BPSD), and the evidence for their use.

BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA (BPSD)

- BPSD can include:
  - Physical aggression
    - Resistiveness or rejection of care
    - Agitation
  - Apathy
  - Inappropriate sexual behavior
  - Sundowning
  - Wandering
  - Rummaging
- Mood disorders
  - Depression
  - Anxiety
- Sleep disturbances
  - Sleep during the day
  - Up at night
- Psychotic symptoms
  - Delusions
  - Hallucinations

BPSD IMPACT

Patients

- Leads to a poorer quality of life
- Risk of injury
- Functional decline
- Risk of admission into nursing home

Caregivers

- Increases time spent doing care
- Increases cost of care
- Risk of injury
- Burnout

BPSD: ASSESSMENT AND EVALUATION

ASSESSING BEHAVIORS: DICE MODEL

- Describe the behavior
- Investigate the influence of:
  - Cognitive status
  - Environment
  - Caregiver approach
  - Physical/medical needs
  - Psychiatric symptoms
- Create a plan
- Evaluate if it works
  - (Kales, Gitlin, Lyketsos, 2014, JAGS)

NPI-Q

- Neuropsychiatric Inventory Questionnaire (NPI-Q) provides a quick assessment of BPSD symptoms
  - Can be completed by caregiver, caring for person with dementia
  - Yes/No Format: There is a point scale to rate severity and distress if answer is yes
    - SEVERITY of the symptom (how it affects the patient)
      - 1 = Mild (noticeable, but not a significant change) to 3 = Severe (very marked or prominent, a dramatic change) points
    - Rate the DISTRESS you experience due to that symptom (how it affects you, the caregiver)
      - 0 = Not distressing at all to 5 = Extreme or Very Severe (extremely distressing, unable to cope with)

NPI-Q SYMPTOMS

- Agitation
- Aggression
- Delusions
- Hallucinations
- Wandering
- Anxiety
- Depression/Dysphoria
- Elation/Euphoria
- Apathy/Indifference
- Disinhibition
- Motor disturbance
- Nighttime behaviors
- Appetite/Eating

NPI-Q USES

- Impact of behaviors on caregivers
  - It is a way to quantify behaviors that caregivers may not realize are even part of the dementia
  - Allows the caregivers to rate behaviors even when they cannot freely talk about the behaviors in front of the patient
- Shows you if behavioral interventions or medications are helpful over time
  - Allows you to see the score decrease if the medication or behavioral intervention is successful.
- Information available at: http://npitest.net
    -

LL: CASE STUDY

- LL is a 92-year old male who lives with his wife
  - Referred to you due to increasing confusion
    - When talking about the patient's confusion, he notes he is "losing his marbles"
      - MOCA score was 18/30
    - Wife tells you he gets angry at times, which he completely denies
  - Walks very slowly with walker, mostly continent, feeds himself
- Live in a one-story house
  - Have no caregivers
    - Son buys them groceries and other necessities
    - Daughter comes to help clean the house each weekend
  - Wife ambulates slowly with a walker, has poor vision due to macular degeneration
    - She does the cooking and helps him bathe

LL: CASE STUDY

- PMH
  - Depression
  - Vascular Dementia
  - OA
  - HLD
  - BPH
  - GERD
  - CAD with CABG
  - CHF
  - Aflutter/AFIB

- Medications
  - Colace 100 mg PO QD
  - Coumadin 2.5 mg PO QD
  - Simvastatin 40 mg PO QD
  - Paroxetine 20 mg PO QD
  - Furosemide 20 mg PO QD
  - Metoprolol 25 mg PO BID

LL: CASE STUDY USING THE NPI-Q

- Delusions: YES
  - Does the patient have false beliefs, such as thinking that others are stealing from him/her or planning to harm him/her in some way?
- Hallucinations: YES
  - Does the patient have hallucinations such as false visions or voices?
  - Does the patient seem to hear or see things that are not present?
- Agitation/Aggression: YES
  - Is the patient resistive to help from others at times, or hard to handle?
- Anxiety: YES
  - Does the patient become upset when separated from you?
  - Does the patient have any other signs of nervousness such as shortness of breath, sighing, being unable to relax, or feeling excessively tense?
- Disinhibition: YES
  - Does the patient seem to act impulsively, talking to strangers as if he/she knows them, or saying things that may hurt people's feelings?

LL: CASE STUDY

- The wife had a plumber over a few months ago to fix the clogged sink.
- The husband now believes she is having an affair with the plumber.
  - Has vivid hallucinations of the plumber and her together.
  - He put kitchen knives in his walker seat and next to his bed to keep the man from trying to kill him, as he tells you he wants to "steal his wife", and "he will stop at nothing to get me out of the picture".
  - Has a baseball bat that he keeps near the front door to "bash" the plumber if he comes in the door, as he will hear him talking outside the window, mocking him.
  - He tells his wife over and over, "I never thought you would do this to me", which makes her feel terrible.

LL: CASE STUDY

- Psychotic symptoms: Delusions, hallucinations (both visual and auditory), and paranoia
- How dangerous is this situation?
  - APS referral?
  - Police?
  - 5150?

MEDICATION REVIEW AND DEPRESCRIBING

ISSUES WITH MEDICATIONS IN DEMENTIA

- Individuals with dementia have an increased risk of cognitive and behavioral effects from medications.
  - Best practice is a medication review for all patients.
  - Unnecessary and potentially damaging medications should be stopped.

The 4Ms of an Age-Friendly Health System

✓ What Matters:

Understanding what each patient's health goals and care preferences are across settings to know and align care, including (but not limited to) end-of-life

✓ Medication:

If medications are necessary, using age-friendly medications that do not interfere with What Matters, Mentation, or Mobility

✓ Mentation:

Preventing, identifying, treating, and managing dementia, depression, and delirium across care settings

✓ Mobility:

Ensuring that older adults move safely every day to maintain function and do What Matters to them

MEDICATIONS: DEPRESCRIBING

- Stop one medicine at a time
  - If problems develop, then it is easy to identify the likely cause
- Taper medicines
  - Some therapies should not be stopped
- Duration of use
  - What are current guidelines?
- Adherence/ Noncompliance
- Consider the "prescribing cascade"

TOOLS: BEERS CRITERIA

- Dr. Mark H. Beers, with 12 experts (geriatricians, psychiatrists, pharmacists), published in 1991.
  - First one was meant for nursing home residents, now includes older adults in all healthcare settings
    - Revised in 1997, 2003, 2012, 2015, and 2019
    - Now done by AGS.
- Lists of potentially inappropriate medications (PIM) for older adults

TOOLS: BEERS CRITERIA

Medications as a group

- Anticholinergics
- Alpha blockers
- Amiodarone
- Spironolactone
- Sulfonylureas
- Reglan
- Sliding scale insulin
- Megestrol and estrogen

Meds causing syndrome

- SSRIs (SNRIs)- falls, SIADH
- BZD- falls, delirium
- Z drugs- falls
- Antiepileptics-falls, syncope
- Dextromethorphan/Quinidine- falls
- Delirium: Antipsychotics, BZD, Steroids
- Dementia: Anticholinergics, BZD
- Falls: SSRIs, Z-drugs, TCA's, SNRIs, opioids

TOOLS: BEERS CRITERIA

- Antipsychotics have their own special category.
  - Anticholinergic
  - Falls and fractures
  - Greater rate of cognitive decline
  - Increased risk of stoke/death
    - This means any antipsychotic is a PIM as soon as you try it
    - All other modalities should be tried first

ANTICHOLINERGIC SENSITIVITY

- The central nervous system (CNS) is likely to have more anticholinergic effects as we grow older. This is due to:
  - Decrease in cholinergic neurons & receptors in the brain
  - Change in drug pharmacotherapy in older adults
    - Decreased hepatic metabolism
    - Decreased renal excretion
    - Increase in blood–brain barrier permeability

ANTICHOLINERGIC RESEARCH

- JAMA, 2015: Study showed people taking anticholinergic drug more than 3 years had a 54% higher risk of dementia vs. people taking the same drug for 3 months
- BMJ, 2006 until 2015: Study of 4,000 subjects, aged 65 to 99 years old
  - Antidepressants (paroxetine), Parkinson meds, antipsychotics, and urologics (oxybutynin and tolterodine) were associated with incident dementia
    - These relationship was noted for exposures 15-20 years prior to the diagnosis of dementia
    - Interesting finding: Antispasmodics, muscle relaxants, & COPD meds were not associated with dementia in the study

Rudolph JL, et al. (2008). *Arch Intern Med.*

Score = 3 points	Score = 2 points	Score = 1 point
Amitriptyline	Amantadine	Carbidopa-levodopa
Atropine products	Hydrochloride	
Benztropine	Baclofen	Entacapone
Carisoprodol	Cetirizine	Haloperidol
Chlorpheniramine	Cimetidine	Methocarbamol
Chlorpromazine	Clozapine	Metoclopramide
Cyproheptadine		Mirtazapine
Dicyclomine	Cyclobenzaprine	
Diphenhydramine	Hydrochloride	
Fluphenazine	Desipramine	Paroxetine
Hydroxyzine hydrochloride &	Loperamide	Pramipexole
hydroxyzine pamoate	Loratadine	Quetiapine fumarate
Hyoscyamine products		
	Nortriptyline	
Imipramine	Olanzapine	Ranitidine
		Risperidone
Meclizine		
	Prochlorperazine	
Oxybutynin	Pseudoephedrine &	Selegiline
Perphenazine	Triprolidine	Trazodone
Promethazine	Tolterodine tartrate	
Thioridazine		Ziprasidone
Thiothixene		
Tizanidine		
Trifluoperazine		

MEDICATION DEPRESCRIBING TOOLS

- STOPP Frail: reviews medications that are potentially inappropriate in frail older patients with less than one-year life expectancy.
  - Age & Ageing. 2017 Jul 1;46(4):600-607
- Medstopper: Allows you to enter a drug list for a specific patient and receive recommendations regarding which medications might be discontinued or switched to safer alternatives
  - www.medstopper.com

LL: CASE STUDY

- Medication Review
  - Colace 100 mg PO QD
  - Coumadin 2.5 mg PO QD
  - Simvastatin 40 mg PO QD
  - Paroxetine 20 mg PO QD
  - Furosemide 20 mg PO QD
  - Metoprolol 25 mg PO BID

- Which medications would you consider as potentially inappropriate?
- Are any of these medications making him worse?

MEDICATION MANAGEMENT OF BPSD

MEDICATION MANAGEMENT OF BPSD

- Management of BPSD symptoms is difficult
  - No FDA approved therapies for BPSD
  - Everything I am about to discuss is OFF LABEL
    - I have no conflicts of interest
- Traditionally antipsychotics are used for BPSD
  - This class has the most adverse side effects for this population

Therefore, there has been a push to find safer medications to use, but unfortunately, evidence for their use in BPSD is also mixed.

MEDICATIONS: PAIN MANAGEMENT

- Pain should be considered whenever a patient has BPSD related to care (bathing, toileting, dressing), or there are increased vocalizations or restlessness
- It is estimated that up to 50% of PWD have pain regularly (ex: OA/OP, Post-stroke)
- Use an assessment tool designed for cognitively impaired to assess for this (PAIN-AD or CNPI- Checklist Nonverbal Pain Indicators)
  - Consider prescribing analgesics routinely to see if this reduces the behavioral issues
  - Start low, but use enough to adequately treat pain
  - Monitor for side effects (sedation/falling) and effectiveness

MEDICATIONS: CHOLINESTERASE INHIBITORS

- Mechanism of action: Cause an enzyme to inactivate, leading to acetylcholine build-up
- Differences in the meds
  - Frequency of dosing: Donepezil QD vs. Rivastigmine oral BID/Galantamine BID
  - Incidence of side effects: Rivastigmine (not patch)> Galantamine > Donepezil
    - Rivastigmine: Works in the cholinergic system, others in liver (P450)
    - Galantamine: Available OTC (Herbal supplement made from flowers) or as a prescription

MEDICATIONS: CHOLINESTERASE INHIBITORS: SIDE EFFECTS

- Salivation, lacrimation, urination, diarrhea (SLUD)
  - Literally do the opposite of anticholinergic meds
- GI side effects: Nausea, vomiting, anorexia/weight loss, diarrhea
- Heart: Syncope, Hypotension, Bradycardia
- Insomnia
- Muscle cramps

MEDICATIONS: CHOLINESTERASE INHIBITORS

- Donepezil: Cochrane Review of 15 RCTs.
  - Small benefits in BPSD
  - Study showed more benefits in cognition and function
    - The 23 mg dose showed more benefit for cognition, but also more side effects.
- Galantamine: Only the 16mg dose showed a small improvement in the Neuropsychiatric Inventory (NPI) scale
- Rivastigmine: 2 studies found improvements in BPSD
  - Also decreased the use of other psychotropic medications in one study
- In summary: Cholinesterase inhibitors may help in BPSD in AD and Lewy Body Dementia, so they are worth a try

MEDICATIONS: MDNA RECEPTOR AGONIST

- Mechanism of Action: Decrease glutamate, which is thought to prevent cell death
- One drug in this class: Memantine
- Side effects: Mild
  - Neuro: Agitation, dizziness, hallucinations, insomnia, confusion, headache
  - Urinary incontinence, diarrhea
- Studies: One RCT showed no difference in BPSD symptoms, another study showed a significant difference in BPSD

MEDICATIONS: DEXTROMETHORPHAN/QUINIDINE

- Approved for pseudobulbar affect
  - There was a 10-week RCT (220 patients) that studied agitation in Alzheimer's disease
    - Cummings JL, et al. (2015). 2015, JAMA.
  - Showed an improvement in agitation/aggression on the NPI (only 1.5 pt. difference)
  - Side effects: GI, dizzy, weakness, edema, fainting
- In summary: Can consider this agent for significant agitation if other meds do not help
  - Keep in mind the interactions with CYP2D6 (other psychotropics)
  - This medication is expensive, as it is newly approved

MEDICATIONS: MOOD STABILIZERS

- Mechanism of action: Enhances gamma-aminobutyric acid (GABA), decrease glutamate at NDMA receptors
- Adverse effects:
  - Lamotrigine: Serious rash (BBW), & dizzy, N/V/Abd pain, ataxia, anxiety, dry mouth
  - Carbamazepine: Aplastic anemia, agranulocytosis, liver enzymes, & GI
  - Valproic acid: Hepatotoxicity/pancreatitis & GI

MEDICATIONS: MOOD STABILIZERS

- Carbamazepine: 6-week study using low doses in nursing home patients showed an improvement in agitation, but another study found no improvements.
- Valproate: 5 studies found no significant improvement
  - More ADR with treatment
- Gabapentin: One small study showed little benefit
- Lamotrigine: No studies done
- In summary, there is no great evidence for the use of mood stabilizers in BPSD
  - Increased ADR associated with this class

MEDICATIONS: SSRI

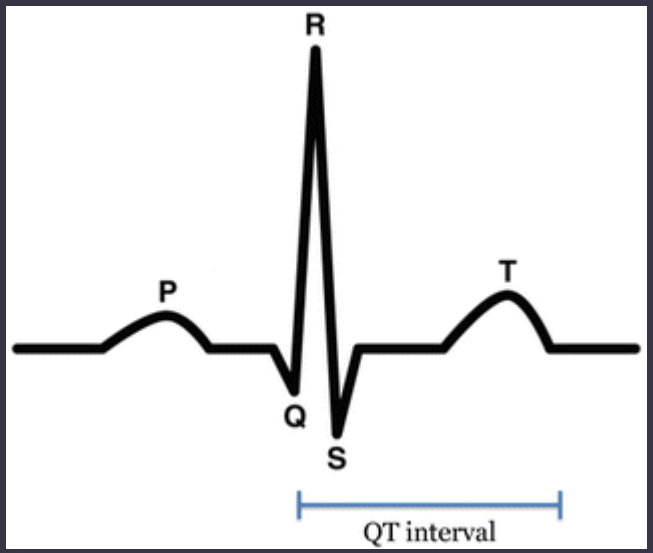
- Mechanism of Action: Work by inhibiting reuptake of serotonin in the synaptic cleft (decrease NE, decrease D)
- Citalopram, Sertraline, Paroxetine, Fluoxetine, Escitalopram, Fluvoxamine
  - Trazadone: (SARI) Serotonin Antagonist Reuptake Inhibitor

MEDICATIONS: SSRI

- Side effects:
  - Sexual dysfunction
  - Increase risk of fracture
    - Risk is greater than with steroids or PPI (GLOW study)
  - Akathisia (restlessness)
  - Insomnia/drowsiness
  - Weight gain/ loss
  - Dry mouth, nausea/vomiting, diarrhea

MEDICATIONS: SSRI QT PROLONGATION

- QT prolongation: Citalopram, Escitalopram (dosage limits)
  - QT is the measure of the time between the start of the Q wave and the end of the T wave on the EKG waveform
  - Represents electrical depolarization and repolarization of the ventricles
  - QT increases the risk for ventricular arrhythmias and sudden death
    - Risks: Female and family hx of sudden cardiac death
- Normal QT is less than 0.40 s (≤400 ms) to 0.44s (≤440 ms)
  - "Abnormal" QTc" in males: above 450 ms
  - "Abnormal" QTc" in females: above 470 ms
  - >500 or a change of >60 ms if on SSRI: STOP drug and get a cardiology referral



MEDICATIONS: SSRI

- Serotonin Toxicity: Usually caused by too many serotonin drugs on board
  - Symptoms:
    - Agitation, restlessness
    - D/N/V
    - Tachycardia
    - Hallucinations, overactive reflexes, spasm, tremor, ataxia,
    - Fever
- Serotonin Withdrawal: Abrupt stoppage or insufficient taper
  - Flu like symptoms
  - N/V/D
  - HA, confusion, tremor, vertigo, imbalance
    - Can last 1-4 weeks!

MEDICATIONS: SSRI

- Sertraline: Showed improvement in depression only
- Paroxetine: Not recommended due to anticholinergic side effects
- Citalopram: Studies have shown reduced agitation/aggression and caregiver distress.
  - The CitAD trial showed efficacy for agitation in AD, but citalopram was at 30mg daily (above the recommended dose- BBW for QT).
- Trazadone: No benefit for BPSD (2 trials compared it to Haldol and found no difference in BPSD).
  - Study from 1997 that showed that trazadone lowered anxiety as much as valium after 3 weeks.
  - Promotes sleep
  - Don't forget about priapism as a rare side effect

MEDICATIONS: SSRI

- Fluoxetine: Study compared it to Haldol for BPSD, but no improvement in agitation
- Fluvoxamine (Luvox): 2 studies done, but only one showed improvement
  - Perphenazine (antipsychotic) was given at the same time
- In summary, SSRI antidepressants may be helpful in treating BPSD, but results are mixed
  - Keep in mind that tapering patients off these medications can cause depression, even if they never have been depressed before
  - Help with FTD the most

MEDICATIONS: SNRI

- Mechanism of Action: Inhibit the reuptake of serotonin and norepinephrine
- Side effects:
  - GI disturbances, CNS stimulation, sexual dysfunction
  - Tremor, tachycardia, sweating, increased BP (dose related)
  - Hepatic irritation (Duloxetine)
  - Sexual: decreased libido, anorgasmia
- No studies done to measure the effect of SNRI's on BPSD, but studies did show an improvement in depression symptoms in dementia patients
- Also useful in pain management, which may help reduce agitation in dementia patients with pain

MEDICATIONS: MAOI AND TCA

- MAOI's: Mechanism of Action: Block monoamine from removing NE, S, and some D.
  - Side effects: Dry mouth, N/D/constipation, dizziness, hypotension, sleepiness/insomnia
    - Dietary interactions: The "cheese effect": foods containing tyramine can cause hypertensive crisis
    - Drug interactions: St. John's wort, psych drugs
- TCA's: Mechanism of Action: Work like SNRI's, but much less selective.
  - A1 adrenergic, histamine & muscarinic cholinergic receptor blockade
    - Potent antihistamines
    - Very anticholinergic
    - Act like Ca+ channel blockers (OD is cardiotoxic), inhibit sodium and calcium
- MAOI's and TCA's are NOT recommended in older adults due to their significant side effects
    - Selegiline was the only medication studied with AD
    - Cochrane review of 17 studies showed no benefits for AD, but studies do show a benefit in PD

MEDICATIONS: MIRTAZAPINE

- Mechanism of Action: Non-adrenergic, specific serotonin receptor (NASSA): tetracyclic antidepressant
  - Side effects: Somnolence, mania, seizures, increased appetite (weight gain), constipation, confusion, tremor, dry mouth
  - Onset of action: rapid (1-2 weeks)
- 12-week trial showed improved agitation in BPSD
    - Side effects of this drug were low

MEDICATIONS: BUPROPION

- Mechanism of Action: NE, D (NeDRI)
  - Side effects: Agitation, hallucinations, mania, dry mouth, HA, N, dizziness, constipation, anorexia (weight loss), urinary frequency, SEIZURE (4 x greater than other antidepressants)
  - Avoid in patients with history of liver disease
  - Stimulating antidepressant, so could increase agitation in BPSD
  - Studies: Small study showed no benefit for apathy
    - Maier F, et al. (2020). Bupropion for the Treatment of Apathy in Alzheimer's Disease: A Randomized Clinical Trial. *JAMA Network Open.* 3(5)

MEDICATIONS: BENZODIAZEPINES

- Mechanism of action: Increases GABA, which reduces brain activity
- Side effects: BBW due to sedation, falls, confusion
  - People can build a tolerance to BZDs if they are taken over a long period of time
    - Short acting: Alprazolam (Half life up to 20+ hours)
    - Medium acting: Lorazepam (10-20 hrs.)
    - Long acting: Diazepam (Up to 100 hrs.)
  - If people suddenly stop taking BZDs, they may get severe withdrawal symptoms (anxiety)
    - Taper off slowly, which can take years

MEDICATIONS: BZD

- In summary, benzodiazepines are NOT recommended for the BPSD of dementia due to their side effects and dependence
  - Meta-analysis (2019) of 10 studies has shown that BZD significantly increases the risk of dementia.
  - Risk is higher in patients taking BZD with a longer half-life (>20 hours) and for a longer duration (>3 years).
    - Use should be limited

      - He, Qian et al. *Journal of Clinical Neurology.*

MEDICATIONS: BUSPIRONE

- Mechanism of action: Partial serotonin agonist. Weak dopamine antagonist.
- Side effects: Dizziness, sleepiness, HA, N, restlessness
- When used for anxiety, it takes > 2 weeks to work
  - No abuse potential
  - Dosed 2-3 times a day
- Small study showed benefit in aggression and agitation.
  - Santa Cruz MR, et al. (2017) Buspirone for the treatment of dementia with behavioral disturbance. Int Psychogeriatrics. May;29(5):859-862.

MEDICATIONS: ANTIPSYCHOTICS

- Mechanism of Action: Calm agitation or aggression through sedation by depleting dopamine, which leads to side effects:
  - Decreased cognitive function, and possible acceleration of cognitive decline
  - Increased risk of falls
  - Increased risk of stroke and of death; this has been estimated as an increased absolute risk of up to 4%
  - Extrapyramidal symptoms, which include stiffness and tremor (Parkinson's like), as well as a variety of other muscle coordination problems
- People with Lewy Body Dementia or a history of Parkinsonism may be especially sensitive to antipsychotic side-effects (Dopamine deplete at baseline)
  - Quetiapine is considered the safest choice

MEDICATIONS: TYPICAL ANTIPSYCHOTICS

- Haloperidol: Meta-analysis of 5 studies showed some improvement in aggression (but not agitation) at a dosage 1-3 mg/day.
  - Drop-out rates were high due to ADR (worsening cognition, falls and fractures).
- Due to adverse effects, Haldol should only be used for severe psychotic symptoms that are not responsive to other modalities.
  - Studies show there is NO clear evidence for the use of any typical antipsychotic in the treatment of dementia related symptoms.
    - Keep in mind the potential QT prolongation.

MEDICATIONS: ATYPICAL ANTIPSYCHOTICS

- Risperidone: Both 1 & 2 mg doses helped BPSD
  - 2 mg dose had higher ADR.
- Olanzapine: 5 mg helped agitation, aggression, hallucinations and delusions.
  - EPS risk is higher at higher doses.
  - Had more weight gain (diabetes) than other meds in this class.
- Quetiapine: No benefit in 3 studies for BPSD, but helped in one study with psychosis in AD and PD.
- Clozapine (monitoring), Ziprasidone, Aripiprazole: No studies in BPSD.

MEDICATIONS: NEWER ANTIPSYCHOTICS

- Includes lurasidone (Latuda), asenapine (Saphris), iloperidone (Fanapt), brexpiprazole (Rexulti), and cariprazine (Vraylar), Aripiprazole (Abilify)
  - Newer drugs (along with quetiapine) can be used as the primary treatment of major depressive disorder
  - None of these new antipsychotics have been studied in dementia

MEDICATIONS: ANTIPSYCHOTICS

- Numerous studies show **ALL** antipsychotics used to treat BPSD are associated with MI, Stroke, and Death, especially with vascular disease
  - Recent study with 90,000 participants shows that in the first 180 days, mortality was 3.8% for Haldol, 2.5% for olanzapine, 2% for quetiapine
  - Concurrent use of NSAIDs may also increase the risk of stroke
- Risk is higher for the typical vs atypical
- Higher doses mean more risk (3.5 %) of death
    - Maust, DT., et al.(2015). *JAMA psychiatry*, *72*(5), 438-445

MEDICATIONS: Z DRUGS

- Mechanism of Action: non-BZD, GABA (Gamma Aminobutyric acid) agonists, which means they help promote sleep
  - Zopiclone, Eszopiclone, Zaleplon, Zolpidem
    - All work quickly and have short duration of effects (Zolpidem is longest)
- Side effects: complex sleep behaviors (sleepwalking), risk of death, fractures, and falls in older adults
- If your patient is on these drugs, they should be slowly tapered with a goal to discontinue them
  - For safer sleep inducers, consider Melatonin, Trazadone, or Mirtazapine

MEDICATION USE: RECOMMENDATIONS

- Stepwise approach for BPSD
  - Start Cholinesterase Inhibitor if they are not already on one
  - Add Memantine
  - If they seem depressed/anxious/aggressive
    - Try SSRI
    - Might consider mood stabilizer if still having behavior

MEDICATION USE: RECOMMENDATIONS

- If they are not sleeping, try Melatonin, then Trazadone or Mirtazapine
- If they are agitated during the day, you could try Trazadone or Gabapentin in small doses to slow psychomotor agitation as well
  - Consider pain medication if the agitation occurs during activities
- If all else fails, or there is a danger to self others or very psychotic symptoms, consider antipsychotic.
  - You can try to taper them off once they stabilize.

LL: CASE STUDY

- Pharmacologic: I started Quetiapine 12.5 mg mg QHS for his delusions, as he is a potential danger to harm himself and his wife.
  - I gradually increased him to 25 mg twice daily at 3 pm and 9 pm, as this stopped his afternoon sundowning, as this is when his delusions were the worst.
  - I had planned to switch his Paroxetine to Mirtazapine or Sertraline, but the son decided to move the patient and his wife to an ALF out of my area.
- Non-pharmacologic interventions:
  - Removed all the knives/weapons in the house during my visit.
  - Referred to APS
  - Talked to the son and daughter, who had no idea this was happening.
    - They helped support the wife, as she was very distraught and embarrassed her husband would think she was having an affair. This reduced her anxiety and sadness about the situation, as it helped her realize she needed more help with him .

EVALUATION OF DRUG TREATMENTS

MEDICATIONS: EVALUATION

- When using medications, tools like the NPI-Q or the DICE model can help show symptom reduction.
  - Document that you check in with caregivers
    - If a medication is not helping, you should try changing the dose or stopping the medication altogether.
  - Discuss black box warnings, and document that discussion
  - Discuss "off-label" use

SUMMARY

- Dementia results in major physical, emotional, and economic burdens for patients, families, and caregivers.
- Our goal is to help patient and caregivers get through this illness the safest way we can.
  - Stop all potentially inappropriate medications that can make patients worse
  - Only start medications if it is necessary
  - Always use non-pharmacologic alternatives if you are able

REFERENCES

- AGS 2019 Updated Beers Criteria for PIM use in Older Adults, JAGS, 2019, 1-21.
- Whitney, M et al. (2014). Review of antidepressants in the treatment of the behavioral and psychiatric symptoms of dementia (BPSD). Mental Health Clinician. July 2014, 4(4), 183-188.
- Kales, H. C., Gitlin, L. N., & Lyketsos, C. G. (2015). Assessment and management of behavioral and psychological symptoms of dementia. *BMJ (Clinical research ed.)*, *350*, h369.
- Gray, S. L., et al. (2015). Cumulative use of strong anticholinergics and incident dementia: a prospective cohort study. *JAMA internal medicine*, *175*(3), 401–407.
- Rudolph JL, Salow MJ, Angelini MC, McGlinchey RE. The Anticholinergic Risk Scale and Anticholinergic Adverse Effects in Older Persons. *Arch Intern Med*. 2008;168(5):508–513.
- Siris ES, et al. (2011). Failure to perceive increased risk of fracture in women 55 years and older: the Global Longitudinal Study of Osteoporosis in Women (GLOW). Osteoporosis Int. 22(1):27-35.

REFERENCES

- Maust, DT., et al.(2015). Antipsychotics, other psychotropics, and the risk of death in patients with dementia: number needed to harm. *JAMA Psychiatry*, *72*(5), 438–445.
- He, Qian et al. "Risk of Dementia in Long-Term Benzodiazepine Users: Evidence from a Meta-Analysis of Observational Studies." *Journal of Clinical Neurology*. 15,1 (2019): 9-19.
- Cummings JL, et al. (2015). Effect of Dextromethorphan-Quinidine on Agitation in Patients With Alzheimer Disease Dementia: A Randomized Clinical Trial. *JAMA*; 314(12):1242–1254.
- Rickels K, t al. (1993) . Antidepressants for the Treatment of Generalized Anxiety Disorder: A Placebo-Controlled Comparison of Imipramine, Trazodone, and Diazepam. *Arch Gen Psychiatry.* 50(11):884–895.