DIAGNOSIS AND MANAGEMENT OF BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA (BPSD)

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DISCLOSURES

• I have no financial disclosures to make

• I will be discussing off-label use of medications to treat behavioral and psychological symptoms of dementia (BPSD)
OBJECTIVES

• Detail the prevalence of behavioral and psychological symptoms of dementia (BPSD) and recognize their impact on caregivers, people living with dementia, and their communities

• Describe the assessment of BPSD

• Apply evidence-based recommendations for non-pharmacologic and pharmacologic management of BPSD
INTRODUCTION TO BPSD

• COMMON
  • 90% of all people living with Alzheimer’s (AD)
  • Similar if not more prevalent in other dementia types

• RANGE OF POSSIBLE SYMPTOMS
  • Agitation, Psychosis
  • Depression, Apathy, Anxiety
  • Sleep Disturbances, Appetitive Changes

• HUGE PSYCHOSOCIAL IMPACT
  • Patient distress
  • Caregiver burnout
  • 30% of the US economic cost of dementia
MORE ON WHO BPSD AFFECTS...

• Most studies in AD and vascular dementia

• Some BPSD are part of the diagnostic criteria or core features
  • Hallucinations and waxing and waning mental status for dementia with Lewy Bodies (DLB)
  • Disinhibition and apathy for behavioral variant frontotemporal dementia (bvFTD)

• We call them BPSD, but they are also common in MCI

• Caregiver effects: burnout, high rates of depression and anxiety, sleep disturbance, and higher overall distress
BPSD EFFECTS ON PATIENTS

• Emotional distress
• Increased risk of injury and medical complications
• Accelerated cognitive and functional decline
• Increased rate of hospitalizations
• Earlier institutionalization
• Increased risks of abuse and neglect
• Earlier mortality
MORE ON THE SYMPTOMS...

• Many patients will have multiple symptoms
  • overlapping
  • at different times during progression

• Depression tends to be more common early on, or even as a prodrome

• Apathy is most common overall

• If agitation or psychosis present, they are more likely to persist throughout the disease course
PREVALENCE OF SPECIFIC SYMPTOMS

WHITE BARS REPRESENT 95% CONFIDENCE INTERVALS

- Apathy: 49%
- Depression: 42%
- Aggression: 40%
- Sleep disorder: 39%
- Anxiety: 39%
- Irritability: 36%
- Appetite disorder: 34%
- Aberrant motor behavior: 32%
- Delusions: 31%
- Disinhibition: 17%
- Hallucinations: 16%
- Euphoria: 7%

Walaszek (2019), adapted from Zhao et al. (2016).
ASSESSMENT OF BPSD

• Characterize the underlying type of dementia, if possible
  • Might any of this be reversible?
  • Etiology can drive treatment choice and understanding of symptoms

• Going back to our foundations: Take a good history
  • severity, quality, timing, antecedents, consequences, and new or change
  • Structured screens can help: NPI-Q, various borrowed forms for facilities
NPI-Q (NEUROPSYCHIATRIC INVENTORY QUESTIONNAIRE)

- CAREGIVER rated
- Screens for 12 different areas of BPSD/NPS
  - Delusions
  - Hallucinations
  - Agitation/Aggression
  - Depression/Dysphoria
  - Anxiety
  - Elation/Euphoria
  - Apathy/Indifference
  - Disinhibition
  - Irritability/Lability
  - Motor Disturbance
- Rate presence, severity, and caregiver distress due to each symptom
Circle "Yes" only if the symptom(s) has been present in the last month. Otherwise, circle "No". For each item marked "Yes":

a) Rate the SEVERITY of the symptom (how it affects the patient):
   1 = Mild (noticeable, but not a significant change)
   2 = Moderate (significant, but not a dramatic change)
   3 = Severe (very marked or prominent, a dramatic change)

b) Rate the DISTRESS you experience due to that symptom (how it affects you):
   0 = Not distressing at all
   1 = Minimal (slightly distressing, not a problem to cope with)
   2 = Mild (not very distressing, generally easy to cope with)
   3 = Moderate (fairly distressing, not always easy to cope with)
   4 = Severe (very distressing, difficult to cope with)
   5 = Extreme or Very Severe (extremely distressing, unable to cope with)
ASSESSMENT OF BPSD

• Any sudden change in mental status and behavior in a person living with cognitive impairment should be considered possible delirium until proven otherwise.

• Consider medication interactions or adverse effects
  • Theory of unmet needs
    • Is the patient in pain or discomfort?
    • Is the patient constipated? Experiencing urinary retention?
    • Is the patient dehydrated or hungry?
    • GLASSES and/or HEARING AIDS?!
TWO MODELS FOR ASSESSMENT AND TREATMENT

DICE
• Describe the problematic behavior;
• Investigate possible causes of the behavior;
• Create a treatment plan; and,
• Evaluate the outcome of this plan.

TIME
• Registration and assessment phase
  • Examine the patient
  • Obtain previous medical records
  • Collect background information
  • Register BPSD in detailed 24-hour records

• Guided reflection phase
  • Hold one or more case conferences to apply a “cognitive problem-solving method” to each NPS
  • Include assessed facts, interpretations, staff members’ emotions and reactions, actions to take, and evaluation

• Action and evaluation phase
  • Implement and evaluate agreed upon actions

**NON-PHARMACOLOGIC MANAGEMENT FOR PATIENTS**

- Most effective (based on extensive literature review)
  - Structured activities
  - Music therapy
  - Sensory interventions including therapeutic touch

- Data inconclusive
  - Pet therapy
  - Aromatherapy (olfactory impairment?)
ASSISTANCE FOR FAMILIES AND CAREGIVERS

• The evidence base suggests that formal support for family or friend caregivers is best
  • VA has caregiver support program locally
  • REACH VA is an excellent model implemented nationally
  • ADRC or Alzheimer’s Association have programming that varies by locality

• Some data for respite and adult day centers

• For facilities, the best evidence is for formal training
  • Trainings should cover: communication skills, behavioral principles, and trauma-informed and person-centered care
PHARMACOLOGIC MANAGEMENT OF BPSD
FIRST LINE APPROACHES

• Optimize medication regimen
  • Anticholinergic burden, polypharmacy, and the Beers criteria
  • Remove offending meds
• Address pain and schedule Tylenol
  • Up to 3 grams per day in divided doses
GENERAL COMMENTS ABOUT PHARMACOLOGY

• No medications are approved for BPSD in the United States
  • In Europe, risperidone is the only approved agent

• Significant risk – is it worth it to treat?
  • All carry the general risks of worsening cognitive impairment, falls, sedation, and gastrointestinal effects, including weight loss
  • Black box warning for increased mortality with antipsychotics
  • Antipsychotics may increase the risk of falls and fracture by 1.5 to 2.5 times

• Informed consent and documentation is critical

Recommendation: start with antidepressants, but antipsychotics have best efficacy data (generally)
PHARMACOLOGIC CONSIDERATIONS

start low

go slow

but go
START WITH ANTIDEPRESSANT MEDICATIONS

• Safer, but considerably less efficacious than antipsychotics
• Use when you have time, space, and safety to do so

• **citalopram, escitalopram, and trazodone**, have the largest evidence base

• Some data (and lots of anecdotal experience) for **mirtazapine** as well

• Recommend strongly against paroxetine and against fluoxetine

• Positive studies for **duloxetine** in DLB but generally recommend against venlafaxine and TCAs
ANTIDEPRESSANT DOSING

- Citalopram
  - 10mg qAM x1 week, then 20mg qAM x 4 weeks, may increase to 30mg qAM after that if partial response, but should get EKG

- Escitalopram
  - 5mg qAM x1 week, then 10mg qAM x 4 weeks, may increase by 5mg up to 20mg qAM

- Duloxetine
  - 20mg qAM x1 week, then 40mg qAM x 4 weeks, may increase to 60mg qAM for depression or other BPSD, but for pain data suggests efficacy up to 120mg

- Mirtazapine
  - Start 15mg or 7.5mg qHS for 4 weeks, may increase by 7.5mg or 15mg up to 45mg qHS

- Trazodone
  - 25-50mg qHS, may titrate by 25-50mg qDay as tolerated up to 250mg daily, may divide BID or TID
HYPONATREMIA?

• Is it clinically significant?
• If it occurs with one SSRI, most likely to occur with others
• Mirtazapine, trazodone, and bupropion less likely
ANTIPSYCHOTICS: GENERAL CONSIDERATIONS

- Risks of: mortality, falls, and fracture, neutropenia (especially with clozapine), cerebrovascular events, cardiac events, extra-pyramidal side effects (EPSE, motor side effects associated with dopaminergic blockade), metabolic side effects, and venous thromboembolism

- Number needed to harm (NNH)
  - 2015 systematic review by Maust and colleagues
  - Haloperidol = 26
  - Risperidone = 27
  - Olanzapine = 40
  - Quetiapine = 50
  - Most deaths are due to cardiac and infectious causes
PLEASE
DO NOT USE
HALOPERIDOL
(OR OTHER TYPICAL ANTIPSYCHOTICS)
AS A FIRST OPTION!!!!!!!
ANTIPSYCHOTICS

- Among the atypical antipsychotics, **risperidone, olanzapine, and aripiprazole** have the most evidence for efficacy.

- Use **quetiapine** first line for patients with **Parkinsonism**, clozapine for treatment-refractory cases

- Pimavanserin is FDA approved for psychosis in Parkinson’s Disease

- In a head-to-head analysis of the three above, olanzapine was shown most effective at managing agitation

- In the same study, for psychosis **risperidone > aripiprazole >> olanzapine**

Maglione et al., 2011; Reus et al., 2016.)
ANTIPSYCHOTIC DOSING

• Aripiprazole
  • Start 2.5mg qHS, may increase by 2.5mg every 1-2 weeks as needed to 10mg, don’t recommend dividing dose

• Olanzapine
  • Start 2.5mg qHS, may increase by 2.5mg every 1-2 weeks as needed to 10mg, don’t recommend dividing dose

• Risperidone
  • Start 0.25mg qHS, may increase by 0.25mg every 1-2 weeks up to 1mg qHS, may divide BID

• Quetiapine
  • Start 25mg qHS or 12.5mg divided BID, may increase by 25mg every 1-2 weeks up to 100-200mg total per day; I sometimes divide TID
DEMENTIA TYPE-SPECIFIC RECOMMENDATIONS

• Dementia with Lewy Bodies and Parkinson’s Disease Dementia
  • Acetylcholinesterase inhibitors have decent evidence to support
  • Donepezil is widely recommended as first-line for BPSD in this population

• Frontotemporal Dementia
  • DO NOT use acetylcholinesterase inhibitors
  • Antidepressants have some evidence base, specifically SSRIs and trazodone
  • Topiramate for hyperorality and hyperphagia
OTHER PHARMACOLOGIC OPTIONS

• Prazosin
• Dextromethorphan-quinidine*
• Methylphenidate and bupropion in apathy
• Trazodone for sleep, data for melatonin/ramelteon not great
• Gabapentin
• Data supports carbamazepine, NOT VALPROATE
HOW LONG SHOULD WE CONTINUE TREATMENT?

• Taper or gradual dose reduction (GDR) should be planned and attempted when possible, or documentation of reasons why it is contraindicated should be completed.

• APA Practice Guidelines recommend attempt at GDR by 4 months
  • These symptoms fluctuate, may not even be present in 4 months w/wo tx
  • Unless prior attempts to taper were unsuccessful
  • OR patient/surrogate don’t want to risk it
THANK YOU!

QUESTIONS?

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