Pharmacologic Management of Dementia-Related Behavior Problems

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Objectives

- Identify behaviors associated with dementia
- Identify drug classes used to treat behavioral disturbance
- Identify risks of antipsychotic use in those with dementia
- Mechanisms to reduce the use of antipsychotic medications in those with dementia
Behavioral Disturbance

- Occur, at some point, in the vast majority of those who suffer from dementia
- 90% of those with dementia
- 75% nursing home residents; greater than 1/2 with 2 behavioral problems
- All stages of dementia
Behavioral Disturbance

- Results in caregiver stress, institutionalization, hospitalization
- Increased agitation as cognitive abilities diminish
- Pre-morbid personality problems
Most Common

- Agitation, depression, psychosis
  - non-aggressive agitation:
    Verbal: constant attention request, complaints, screaming
    physical: pacing, disrobing, out of chair/bed
  - aggressive agitation:
    verbal: threats, name calling
    non-verbal: biting, hitting, pushing, scratching
  - Resisting care
Behaviors cont’d

- Sleep disturbance
- Wandering
- Delusions, hallucinations, depression, sleep disturbance may underlie behavioral agitation
Loneliness

- Have the patient interact with someone he/she has a positive and loving relationship with
- One-to-one
- Animals
- Massage
- Tapes/videos of loved ones
Boredom

- Stimulation needed
- Sensory stimulation-aromatherapy, music, touch, books, items like buttons/snaps to manipulate
- Meaningful activities such as folding laundry, cooking, cleaning
Psychosis

- Delusions and hallucinations
- Paranoia may be most prominent in the middle stages of dementia
- Delusions of theft, breaking in, food poisoned
- Visual hallucinations include animals, intruders, complex scenes, people from the past
Depression

- Depression in about \( \frac{1}{2} \) of those with dementia
- Different from apathy-psychic distress and low mood
- Often goes unnoticed in the presence of agitation
Anxiety

- May be more prominent in earlier stages
- Adjustment to increased dependency and functional decline
- Fuels behavioral problems
Sundowning

- Early evening increase in psychiatric/behavioral symptoms
- May be related to change in sleep patterns, loneliness, decreased social and physical time cues
- Medications not first line approach
Disruptive Vocalizations

- May be associated with anxiety, depression, physical discomfort, or other environmental factors
- Consider music if patient feels isolated/lack of stimulation
- Reinforce-reward quiet behaviors and appropriate help seeking behavior
Sleep Disturbance

- SD in 30%-56% of those with AD
- With age, decrease in REM and slow wave sleep, increased nighttime wakefulness
- Decreased daytime activity, depression, sleep apnea, restless leg syndrome
- Bright light therapy, melatonin, increase exercise, proper sleep environment, decrease pm caffeine/ETOH, later bed time
Sleep Disturbance

- SD in AD patients associated with caregiver burnout
- May precipitate or worsen day time agitation, irritability, aggressive behavior
- May interfere with function and cognition
- May increase risk for falls/traumatic injury
Sleep Disturbance

- Garcia-Alberca et al (2013) found SD to be associated with depression, disinhibition, aberrant motor behavior - those with galantamine treatment showed less SD
Self-Injurious behavior

- Self-induced skin excoriations
- Consider delusions as contributory factor
- Physical barrier
Hoardings

- Collecting a large number of unneeded objects
- Patient can become agitated and violent if others threaten to remove objects
- Provide areas that they can safely acquire objects from
- Consider providing a storage area
Sexually Inappropriate Behaviors

- “Sex talk”
- Sex acts-exposing, grabbing, fondling
- Behavioral approach
- Antidepressants, antipsychotics, cholinesterase inhibitors, gabapentin
Emergent Behavioral Disturbance

- Suicidal behaviors
- Physical assault on others
- Profound weight loss secondary to depression
- Refusing life sustaining medications
- Risk of self harm
Primary Behavioral Disturbance

- Caused by underlying neurochemical changes related to the disease that is causing dementia
Secondary Behavioral Disturbance

- Caused by co-morbid medical issues, delirium, medications, pain, environment, unmet personal needs
Mixed Behavioral Disturbance

- A primary behavioral disturbance may be exacerbated by a secondary factor.
Less Likely to Respond to Medications

- Wandering
- Hoarding
- Apathy
- Repetitive verbalizations
- Situation specific behaviors
Why Treat Behaviors

- Significant emotional distress to caregivers and patients
- Increase hospitalizations, institutionalization, caregiver burnout
- Can be dangerous or even life-threatening
Treatment

- NO FDA approved medication for behavioral disturbance associated with dementia
- Strongest evidence for antipsychotics in the treatment of behavioral disturbance, SSRI’s next
- Inconsistent evidence for anti-epileptics
- Studies usually 12 week or less
American Psychiatric Association

- Recommend antipsychotics for agitation based on current evidence
- Consider anticonvulsants, Lithium, beta blockers, SSRI (agitated non-psychotic)
Anti-Dementia Medications

- Cholinesterase inhibitors
- Donepezil, galantamine, rivastigmine
- May be useful in those with behavioral symptoms in the setting of mild-moderate dementia
- Studies have conflicting results
- Double blind placebo controlled trial of patients with LBD showed reduced hallucination/improved cognition with rivastigmine
Anti-Dementia Medications

- Memantine-?
Risks of Cholinesterase Inhibitors

- donepezil, rivastigmine, galantamine
- GI side effects such as nausea, poor appetite, weight loss, diarrhea, caution with PUD
- potential cardiac conduction slowing: caution with cardiac conduction delays, bradycardia, syncope
- Caution with asthma and COPD as bronchial secretions can be increased
SSRI

- Citalopram can be helpful with agitation and paranoia in patients with Alzheimer’s dementia.
- Often symptoms driven by underlying mood disorder.
- Consider short term antipsychotic, if needed, until SSRI becomes efficacious.
A 12 week RCT comparing citalopram and risperidone in dementia patients with agitation showed similar efficacy; less adverse effects with citalopram (n=103).
SSRI

- QT prolongation with citalopram; do not use greater than 20 mg daily in those over 60 y/o
- Serotonin deficits may contribute to behavioral disturbance in those with frontotemporal dementia
Antidepressant side effects

- Anxiety
- GI distress (sertraline), poor appetite/increased appetite, headache, sexual dysfunction, sweating, hyponatremia, dry mouth/constipation (paxil), nightmares, sedation, insomnia
- Bleeding with SSRI: inhibit platelet function
Antidepressants

- Increased risk of suicidal ideation/behaviors
- Venlafaxine: hypertension, nausea
- Remeron: sedation, weight gain, rare neutropenia, less sexual dysfunction
- Bupropirion: anxiety, dizziness, insomnia, tremor
- Duloxetine: nausea, poor appetite, sweating
Antidepressants

- Trazadone: sedation, increased appetite, orthostasis, dizziness, headache, priapism
Serotonin syndrome

- Hyperstimulation of serotonin receptors
- Nausea, diarrhea, restlessness, agitation, hyperreflexia, autonomic instability, myoclonus, hyperthermia, rigidity, seizure
Antiepileptic drugs

- Carbamazepine
- Valproate
- Gabapentin
- Lamotrigine
Antiepileptics

- Carbamazepine has been shown to be effective for short term control and agitation.
- Ataxia, drowsiness, postural instability, rash, weakness, disorientation more common in carbamazepine group.
Antiepileptic side effects

- Carbamazepine: rash, SIADH/hyponatremia, aplastic anemia, liver enzyme abnormalities
- Valproate: liver toxicity, pancreatitis, thrombocytopenia, GI discomfort, sedation
- Lamictal: rash
- Neurontin: sedation, peripheral swelling, dizziness, coordination problems, fever
Analgesia

- Consider a protocol to assess and treat pain
- Can reduce agitation that is driven by pain/discomfort
Antipsychotics

- RCT’s have shown risperdal and zyprexa to improve aggression scores
- Most commonly used: seroquel, risperidone, olanzapine
- aripiprazole, clozaril
- Not FDA indicated for dementia related psychosis or behavioral disturbance
Black Box Warning

- Initial warning in 2003: Increased risk of cerebrovascular events, including stroke, in dementia patients receiving risperidone; relative risk about 2
- FDA 2005: based on a meta analysis of 17 trials using atypical antipsychotics in elderly patients with dementia related psychosis. Increased mortality risk with atypicals compared to placebo
- Relative risk of 1.6-1.7 for mortality related to mainly cardiovascular events or infection
Black Box Warning

- "Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk for death"
- Warning extended to first generation antipsychotics
Omnibus Budget Reconciliation Act

- 1987
- Increased monitoring of antipsychotic use in nursing homes
- Must document appropriate diagnosis/target symptoms, symptoms change over time, SE monitoring, concurrent behavioral treatment
- One attempt every 6 months at dosage reduction—or document rationale for not doing so
January 2007 iteration of OBRA

- GDR-gradual dose reduction of all antipsychotics in NH
- During 1st year of treatment must document at least 2 attempts at reduction with at least one month between attempts
- After first year, one GDR yearly unless contraindicated
- Documentation of contraindicated GDR: target sx worsened with most recent GDR in current facility AND physician’s opinion why further GDR likely to impair function or worsen target symptoms
Antipsychotic side effects

- QT prolongation
- Extrapyramidal symptoms
- Metabolic syndrome: weight gain, increased waist circumference/TG/glucose, increased BP, decreased HDL
- Somnolence (may decrease over time)
- Stroke (conflicting data)
- Myocardial infarction
- Death (black box warning)
- Hyperprolactinemia (increased risk for osteoporosis)
Antipsychotics

- Anticholinergic effects: constipation, dry mouth, blurred vision, urinary retention (clozapine, olanzapine)
- Orthostatic hypotension: clozapine, quetiapine, risperidone, olanzapine
- Clozaril: agranulocytosis, drooling, seizure
Extrapyramidal Symptoms

- Increased likelihood with typicals - stronger dopamine D2 receptor blockade
- Akathisia (restless, anxiety, agitation)
- Dystonia (tonic-clonic contractions, spasms, rigidity)
- Parkinsonism (bradykinesia, rigidity, tremor)
Cardiac Side-effects

- QTc interval (depolarization and repolarization of heart ventricles) can be increased
- Increase QTc increases risk for arrhythmia
- Geodon is the atypical antipsychotic with highest risk for QTc prolongation
- Oral haloperidol lowers risk of QTc prolongation (IV higher risk)
Tardive Dyskinesia

- Abnormal involuntary movements
- Can be permanent
- Examples: grimacing, chewing movements, tongue thrusting, swaying of hips/trunk
- Can be rhythmic or choreiform
Neuroleptic Malignant Syndrome

- High fever, rigidity, altered mental status, autonomic instability (HTN, tachycardia, sweating)
- Can be fatal
Benzodiazepines

- Lorazepam, diazepam, tamazepam, alprazolam, clonazepam
- Cognitive impairment, sedation, falls, disinhibition, delirium, withdrawal, psychomotor impairment, physical dependence
- Paradoxical agitation
- Suggest limited short term use only (2-4 weeks), if must use
- 10% geriatric hospitalizations related to benzodiazepine use (Voyer & Martin, 2003).
Falls

- Increased risk with psychotropics
- Recent retrospective study (n=404) in the Netherlands found psychotropics associated with increased fall risk
  - antipsychotics: odds ratio 3.62
  - hypnotics/anxiolytics: OR 1.81
  - short acting benzodiazepines: OR 1.94
  - antidepressants (esp. SSRI): OR 2.35
Fractures and Psychotropics

- In white populations over 50 years old, 50% women and 20% men will sustain osteoporotic fracture in their lifetime.
- 2005: cost of osteoporotic fractures estimated at $17 billion.
Fractures

- SSRI associated with lower bone mineral density and increased risk of fracture
- Conflicting evidence regarding risk of fracture in relation to treatment with antipsychotics and benzodiazepines.
- Lithium may protect against fragility fractures
Considerations

- Investigate prior to initiating treatment with antipsychotics
- Pain often overlooked as basis for behavioral disturbance
- Cognitive impairment and communication issues impair ability to articulate complaints
Considerations

- Underlying medical issues such as urinary tract infection, dehydration, adverse drug reactions, polypharmacy, fecal impaction, tooth pain, fracture, congestive heart failure.
- Delirium
- High degree of suspicion, familiarity with patient, early recognition and treatment
- Medication side effects (esp anticholinergic)
Considerations

- Environment
  - noise
  - routine change
  - lack of activity/engagement
  - adequate staff to meet basic needs
  - high caregiver turnover
  - limiting group number
Behavioral Approach First

- Optimize sensory input (glasses, hearing aide)
- Maximize patient’s autonomy/need for control
- Physical activity
- Compromise
Evidence Based Approaches

- Care giver psychoeducation/support
- Music therapy
- Cognitive stimulation therapy
- Controlled multisensory stimulation
- Staff training/education
Wandering

- Lock doors
- Wander guards
- Wander gardens
- Patterns to redirect
Sexually Inappropriate Behaviors

- Reminders
- Private room
- Clothing modification
Clear Indication for Medicating

- Behavioral emergency
- Risking safety of self/others
- Behavioral approaches have failed
- Patient continues to appear uncomfortable and distressed