

THE ALZHEIMER'S PROJECT



LIVE WELL
SAN DIEGO

Pharmacological Management of Behavioral & Psychological Symptoms of Dementia

Investigate: Ten Key Points

1. New or rapidly worsening behavioral symptoms in a patient with dementia should be considered a sign of an underlying medical illness until proven otherwise.
2. The first step in evaluation is to assess whether underlying medical factors may be involved.
3. Problem behaviors are often triggered by anticholinergic meds and suboptimal prescribing.
4. Obtain a careful history focused on any changes in the patient's medical status and medications.



Investigate: Ten Key Points

5. There are differences between the psychotic symptoms typically seen in patients with dementia versus the psychosis seen other conditions.
6. “Psychobehavioral metaphor” may help select a class of medication most helpful.
7. In certain situations a risk-to-benefit analysis may still favor the use of antipsychotic medications.



Investigate: Ten Key Points

8. Other possibly helpful strategies: prazosin (Minipress[®]) and dextromethorphan-quinidine (Nuedexta[®]).
9. The use of both pharmacological and behavioral strategies leads to the best results.
10. Symptoms evolve over the stages of dementia and may decrease or disappear.

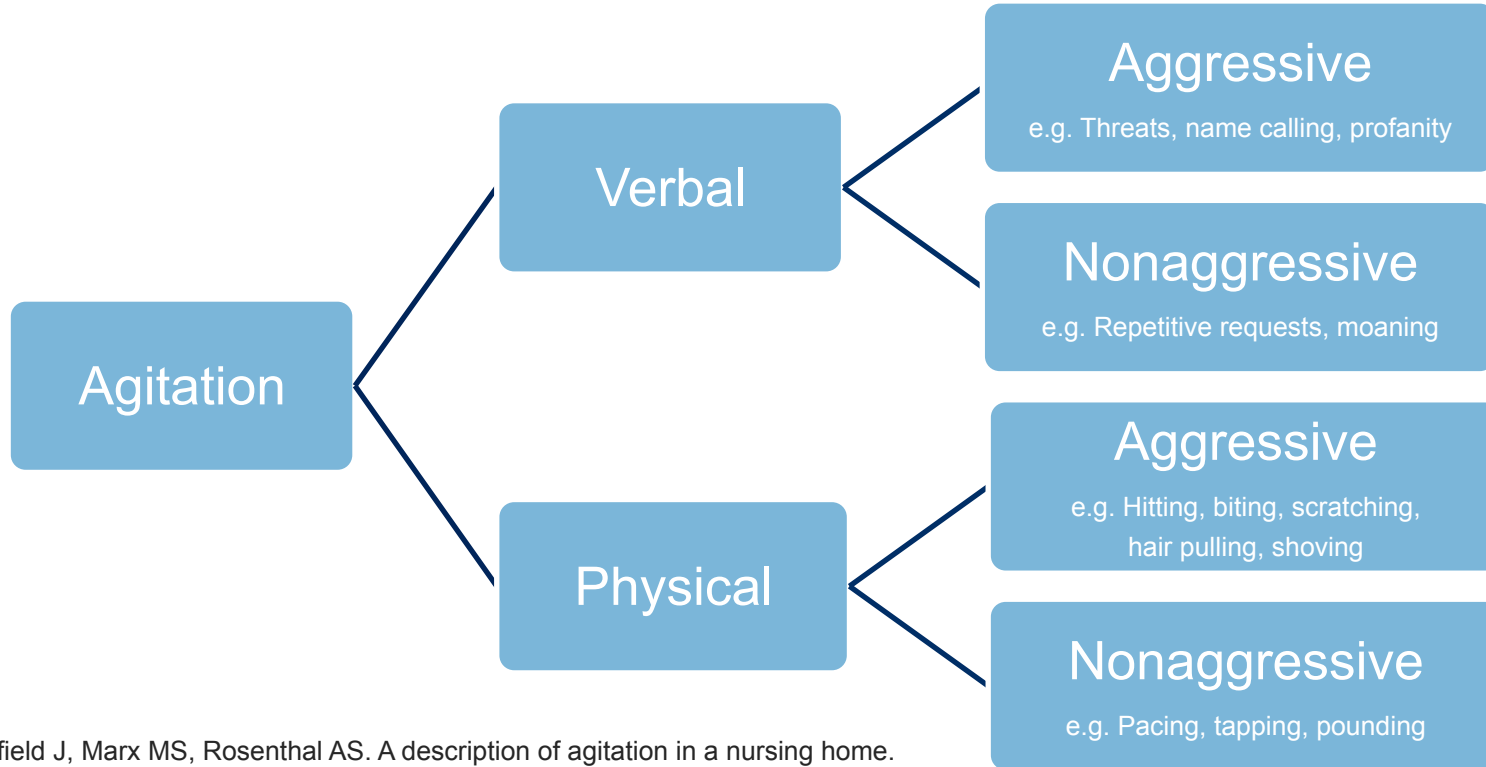


Common Behavioral Problems

- Food Refusal
- Wandering
- Restlessness
- Sleep disturbances
- Combativeness
- Disinhibition
- Hypersexuality
- Irritability
- Depression
- Psychosis
- ADL refusal
- Social withdrawal
- Medication refusal
- Anxiety
- Agitation
- Aggression



Types of Agitation



Cohen-Mansfield J, Marx MS, Rosenthal AS. A description of agitation in a nursing home. Journal of Gerontology: Medical Sciences 1989;44(3):M77-M84.

Appropriate Evaluation

Behavioral symptoms in a patient living with dementia should be viewed as a form of communication

- Symptoms often represent the person's best attempt to signal a problem
- Development of symptoms should trigger a careful investigation to determine cause(s)
- Symptoms often an indication of underlying medical problem



Differential Diagnosis:

Patient Related

Causes related to the patient categorized as:

- **Medical:** suboptimal prescribing, uncorrected sensory deficits, hypoglycemia, pain
- **Psychiatric:** depression, anxiety, paranoia
- **Psychological:** frustration, boredom, TV violence, loneliness
- **Other:** thirst, hunger, fatigue, noise, movement restriction

Differential Diagnosis

- New medical conditions
- Pre-existing medical conditions
- Sub-optimal prescribing
- Poly-pharmacology
- Medication nonadherence
- New psychiatric condition
- Pre-existing psychiatric condition re-emerging
- Use of drugs and/or alcohol



Recognizing Delirium

- Have there been any recent medication changes?
- Does the patient look physically ill or physically uncomfortable?
- Are the patient's vital signs reasonable?
- Are the vital signs around their usual baseline?
- Are the patient's lab values reasonable?
- Has mental status changed rather suddenly or dramatically?
- Is the patient suddenly behaving in ways that have never been characteristic for the patient?
- Is the patient's level of alertness and/or attention waxing and waning?

Sub-Optimal Prescribing

- Prescribing a medication from an essential category of medication that is not senior friendly
- Prescribing a dose of an essential medication that is larger than needed
- Prescribing a medication to be taken at a time of day that is not optimal (e.g. diuretics at bedtime)
- Not prescribing a needed medication (e.g. a pain medication)
- Long-term use of opiate pain medication in patients other than those with terminal cancer



Sub-Optimal Prescribing

Poly-pharmacy

- Avoidable morbidity and mortality
- Can be caused by numerous prescribers with limited communications



Sub-Optimal Prescribing

Prescribing Cascade

- Medication addresses problem but creates side effects
- Second medication treats side effects but may cause additional side effects



If no medical issues identified

Look for co-occurrence of psychiatric conditions

- Panic disorder
- Depression
- Manic state
- Paranoid psychosis



DICE APPROACH TO BEHAVIORAL AND PSYCHOLOGICAL SIGNS AND SYMPTOMS OF DEMENTIA

CREATE (TREATMENT)

Psychobehavioral Model

ASSUME patient does
not have dementia

ASSESS psychiatric signs
and symptoms

ALIGN symptoms to best
fit psychiatric syndrome
eg., major depression, paranoid
psychosis, mania, etc.

Pharmacological Treatment of Agitation & Aggression

CREATE (TREATMENT)

If treatment of physical problems and/or behavioral modifications do not control behaviors consider pharmacologic treatment — Examples:

- Irritability/depression - antidepressant
 - Fear/paranoia - antipsychotic
- Disinhibition/embarrassment - mood stabilizer
 - Movement/pain - analgesic

Best Practices for Prescribing

- Use medications better tolerated by older adults
- Older patients often need lower dosages
- Check timing of medication dose against other issues, i.e., diuretics
- Omission of medications
- Opioid pain medication – reduce long term use



Best Practices for Prescribing

Beer's Criteria or Beer's List

- List of medications more harmful than helpful for older patients
- Originally developed in 1997
- Latest versions in cooperation with American Geriatrics Society



Use of Psychotropic Medications

- Track impact of medication
- Start low dosage
- Increase slowly
- Always use lowest possible dose
- Incrementally reduce dose and assess if behaviors return
- Symptoms may recede over disease progression and use of meds may not be necessary
- May be possible to discontinue medication



Use of Psychotropic Medications

- For all classes of psychotropics, preference for medications that are renally excreted
- Benzodiazapine rarely helpful for older patients and should generally be used in a time-limited manner for situational symptoms
- Look for meds with intermediate half-life
- Preferred benzodiazapines:
 - Lorazepam (Ativan[®])
 - Oxazepam (Serax[®])
 - Temazepam (Restoril[®])



Use of Psychotropic Medications

Use PDR as reference tool for:

- Appropriate starting dosage
- Maximum dosage
- Side effects

Antipsychotic Medications

Drug	Dose
Aripiprazole (Abilify)	4 forms including tablets (2, 5, 10, 15, 20, 30 mg), DiscMelt (10 and 15 mg), liquid and IM
Asenapine (Saphris)	2.5 mg & 5 mg sublingual; q12 hours
Cariprazine (Vraylar)	Capsules (1.5, 3, 4.5 and 6 mg)
Clozapine (Clozaril)	Refer to psychiatrist
Iloperidone (Fanapt)	Tablets (1, 2, 4, 6 mg); q 12 hours
Lurasidone (Latuda)	Tablets (20, 40, 60, 80 mg)
Olanzapine (Zyprexa)	4 forms including tablets (2.5, 5, 7.5, 10, 15, 20 mg) Zydys (5, 10, 15, 20 mg), IM, IM ER
Paliperidone (Invega)	Tablets (1.5, 3, 6 and 9 mg) Max = 12 mg, Renal = 3 mg
Pimavanserin (Nuplazid)	Tablet 17 mg (FDA for Parkinson's disease psychosis)
Quetiapine (Seroquel)	Tabs (25, 50, 100, 200 mg) q 12 hours; Extended release tabs (50, 150, 200, 300, 400 mg)
Risperidone (Risperdal)	4 forms including tablets and M-Tabs (0.25, 0.5, 1, 2, 3, 4 mg), liquid, Risperdal Consta (q 2 weeks)

Antidepressant Medications

Drug	Dose
Citalopram	10, 20 and 40 mg tabs (20 and 40s are scored). Starting dose is 10 mg. Max dose = 40 mg. Doses above 40 mg not recommended due to QTc prolongation.
Escitalopram	5, 10 and 20 mg (10 and 20s are scored). Starting dose is 5 mg. Max dose = 20.
Sertraline	25, 50 100 tabs plus oral solution. Starting dose = 25 mg. Max dose = 200 mg.
Duloxetine	20, 30, 60 mg tabs. Starting dose 20 mg. Max dose = 60 mg.

NOTE:

- 1) These are generally considered the best choices for older adults but other factors like previous treatment history or family history may influence your choice.
- 2) If you prescribed any two antidepressant medications for a particular patient without success, then a referral to a psychiatrist is recommended.

Mood Stabilizing Medications

Drug	Dose
Divalproex	Sprinkles 125; , DR 125, 250 500 mg; ER 250 and 500 mg. Oral solution: 250 mg/5 ml. Starting dose = 125 to 250 mg. Dose is determined by clinical response and blood level of total valproic acid (50 to 100 µg/ml). When converting to ER, increase dose by 20%.
Lithium	Tablets, capsules, oral solution; and ER. 300 mg tabs. ER comes in 300 and 450s. Solution: 8 mEq/5 ml. Recommended trough serum range is 0.4 to 0.8 mmol/L. Starting dose = 300 mg.
Gabapentin	Capsules 150, 300, 400 mg; Tablets 600 and 800; liquid. Starting dose 150 to 300 mg; Max dose = 3600 mg in a divided dose.
Pregabalin	Caps: 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, and 300 mg. Oral Solution: 20 mg/mL.



Benzodiazepines

- Rarely appropriate for long-term use
- Helpful for acute agitation
- Short-acting, renally excreted agents are preferred
- Occasionally may use clonazepam (Klonopin[®])
- Small doses (e.g. lorazepam 0.5 mg)
- Worrisome side effects: delirium, clumsiness, falls, depression, tolerance, dependence and withdrawal
- Rapidly disintegrating formulation may be helpful



Other Medications:

Trazodone (Desyrel[®])

- May treat both acute agitation and prevent further episodes
- May be good choice for insomnia
- Dose range: 25 - 100 mg
- Complete response may take 2-4 weeks
- Sedation is common
- Priapism is very rare in older patients



Other Medications:

Prazosin

The noradrenergic system is the brain “adrenalin” system for attention and arousal

Despite the loss of noradrenergic locus ceruleus neurons in AD there is

- Increased CSF norepinephrine (NE)
- Increased agitation response to NE
- Increased alpha-1 adrenoreceptors in locus ceruleus

As a result: Excessive noradrenergic reactivity produces anxiety and agitation and may contribute to agitation in individuals living with AD

Other Medications: Prazosin

- Prazosin is an alpha-1 receptor antagonist
 - The only one that crosses from the blood into the brain
 - Non-sedating
 - Does not cause parkinsonism but may reduce BP
 - Shown to have long-lasting benefits in PTSD
 - **An open label trial and a small placebo-controlled trial have found that it is helpful in treating agitation in NH residents with AD**
 - In AD, dosed between 1-6 mg/day



Dextromethorphan-Quinidine

- Dextromethorphan hydrobromide and quinidine sulfate (Nuedexta[®]) is approved for pseudobulbar affect (PBA) in the US and European Union
- Dextromethorphan is
 - Most well-known as a cough suppressant
 - a low low-affinity, uncompetitive NMDA receptor antagonist
 - σ_1 (sigma₁) receptor agonist
 - Serotonin and norepinephrine reuptake inhibitor
 - Neuronal nicotinic $\alpha_3 \beta_4$ receptor antagonist
- Quinidine
 - is a Class 1 antiarrhythmic
 - When *combined* with *dextromethorphan*, *quinidine* works by increasing the amount of *dextromethorphan* in the body



Dextromethorphan-Quinidine

- Dosing in PBA
 - The combination of dextromethorphan (20 mg) - quinidine (10 mg) comes as a capsule to take by mouth.
 - It can be taken with or without food
 - Starting dose is once a day for 7 days
 - After 7 days, it is taken every 12 hours
 - More than 2 doses should not be taken in a 24-hour period
 - Patients should be sure to allow about 12 hours between each dose
 - Patients should take dextromethorphan-quinidine at around the same time(s) every day
 - **Important drug-drug interactions:** desipramine (levels increase 8-fold), paroxetine (2-fold increase), MAOIs and memantine



ChampionsforHealth.org/alzheimers

Website to be updated regularly with most current information



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