Non-Urgent Treatment of Agitation in Patients with Dementia

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Overview

- Non-urgent agitation refers to distressing symptoms and behaviors that don't immediately jeopardize patient or caregiver safety. Some examples are asking the same questions or making the same statements repeatedly; pacing and fidgeting; resisting care or assistance with ADLs like bathing; constantly talking or mumbling to themselves in a distressed manner; and showing irritability or frustration over minor issues.
- While we usually choose antipsychotics for urgent agitation, we use them more sparingly for non-urgent agitation due to boxed warnings of increased risk of stroke and death in patients with dementia.
- The only FDA-approved medication for agitation in dementia is brexpiprazole, though it's no safer or better than other antipsychotics.
- Risperidone is approved for agitation in Australia and the United Kingdom and is also approved for aggression and psychotic symptoms in Alzheimer's disease in Canada.

Treatment Recommendations

[Note: these recommendations are based in part on the following published algorithms: Chen A et al, Psychiatry Research 2021;295:113641; Davies SJC et al, Journal of Psychopharmacology 2018;32(5):509–523]

1. Constitutional Measures
    a. Review any anticholinergic medications prescribed and reduce their dose or discontinue if feasible.
    b. Optimize sleep, pain, bowel management
        i. Sleep: Melatonin 1 mg to 10 mg 3 hours prior to bedtime
        ii. Pain:
            1. Acetaminophen 325 mg to 650 mg q6h; used for agitation triggered by pain
            2. Morphine 2.5 mg to 10 mg q4h PRN; reserved for patients receiving hospice/palliative care
        iii. Bowel management: walking, prune juice, sennosides/docusate, bisacodyl, polyethylene glycol (MiraLAX), lactulose
2. Antidementia Therapies
    a. If not already initiated, start treatment with an ACEI +/- memantine, as appropriate
3. Antidepressants
    a. Escitalopram 5 mg to 20 mg
    b. Sertraline 25 mg to 200 mg
    c. Trazodone is helpful for frontotemporal dementia; Give 50 mg to 300 mg in divided doses
4. Anticonvulsants
    a. Listed in order of preference:
        i. Gabapentin 300 mg to 900 mg daily in divided doses. Renally dose in patients with kidney insufficiency.
        ii. Carbamazepine 50 mg to 400 mg daily. Monitor for side effects such as dizziness, drowsiness, and balance issues.
        iii. Divalproex/Valproic acid 125 mg qHS to 750 mg daily in divided doses. Often avoided due to sedation/dizziness and other neurotoxic side effects, limit use to situations where other options aren't working.
5. Atypical Antipsychotics
    a. Listed in order of preference:

i. Aripiprazole 2 mg to 15 mg daily
ii. Risperidone 0.25 mg to 2 mg daily
iii. Olanzapine 2.5 mg to 10 mg
iv. Brexpiprazole 2 mg to 3 mg daily; lower doses were ineffective in studies
v. Quetiapine 12.5 mg to 200 mg daily in divided doses;
    1. While a popular choice, it's been less effective in studies.
    2. Quetiapine is a first line choice for treating psychosis in patients with Parkinson's disease dementia or lewy body dementia
vi. Pimavanserin is FDA approved for Parkinson's disease psychosis and has been beneficial for behavioral symptoms in dementia.

6. Combinations of antidepressants, anticonvulsants, and atypical antipsychotics
7. Adrenalin-mediated treatments (limited data, though recommended in recent algorithms)
    a. Prazosin 1 mg to 6 mg daily in divided doses; watch for orthostatic hypotension
    b. Propranolol 10 mg to 100 mg daily in divided doses (Peskind ER et al, *Alzheimer Dis Assoc Disord* 2005;19(1):23–28); watch for bradycardia and hypotension
8. Electroconvulsive Therapy
    a. Trial ultra-brief right unilateral pulses over bilateral ECT initially
    b. Risk of increased confusion