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ELDER CARE

A Resource for Interprofessional Providers

Psychosis in Dementia - Pharmacotherapy

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Psychotic symptoms occur at some point in as many as 23% of older adults. Most of these individuals have secondary psychosis (i.e., the psychotic symptoms are associated with an underlying medical, psychiatric, or neurological disorder). Examples of underlying causes include dementia and other neurocognitive disorders, delirium, mood disorders, and medical illness. Sometimes, psychosis is due to medications or dietary supplements.

Most commonly, however, psychosis in older adults is associated with dementia. Psychosis in these instances is less often characterized by clear-cut psychotic symptoms such as delusional ideation or hallucinosis but rather, inferred from grossly disorganized behaviors. This Elder Care will focus primarily on treatment of dementia-associated psychosis. Treatment poses a challenge because there are no medications that reverse the course of dementia.

Management Goals

Psychotic symptoms in demented patients typically come to clinicians' attention because of disruptive behaviors. The goal of treatment is to contain such behaviors, especially when they pose a risk to the patient or others. The first line of treatment is non-pharmacologic. This includes minimizing sensory deficits; addressing possible contributing factors such as pain and constipation; creating a structured, predictable environment; and, importantly, modifying or discontinuing any concurrent medications that might cause or aggravate psychosis, such as certain Parkinson's disease medications. Ultimately, however, pharmacologic approaches are often needed. These rely, to date, primarily on antipsychotics, and these drugs can have serious side effects (Table 1).

All antipsychotics now carry a black box warning of an increased mortality in older patients with dementia-related psychosis. The increased risk of death is primarily due to cerebrovascular events. Thus, before prescribing an antipsychotic, clinicians should assess whether the potential benefit of treatment (e.g., preventing injury to the patient or others) outweighs the risk. Medications should not be prescribed simply to control behavior for the convenience of caretakers or staff.

It is also important to distinguish the type of dementia.

Table 1. Adverse Effects of Antipsychotics

Organ System	Adverse Effects
Cardiovascular	ECG changes, orthostatic hypotension, edema, hypertension, syncope, tachycardia
Central Nervous System	Extrapyramidal symptoms (e.g., akathisia, Parkinsonian movements), anxiety, dizziness, fatigue, headache, insomnia, sedation
Gastrointestinal	Abdominal pain, constipation, increased appetite, nausea
Genitourinary	Cystitis, incontinence, sexual dysfunction
Metabolic	Weight gain, dyslipidemia, type-2 diabetes
Neuromuscular	Dyskinesia, myalgia, tremor
Respiratory	Congestion, cough, pneumonia, rhinitis

Patients with Lewy body dementia are at increased risk of serious side-effects from antipsychotic treatment. Patients with vascular dementia may have more risk of adverse cardiovascular effects, particularly when taking antipsychotics that have an intermediate-to-high metabolic risk (Table 2).

Table 2. Metabolic Risk Categories of Second-Generation Antipsychotic Medications

Category	Examples
High	Clozapine, Olanzapine
Intermediate	Quetiapine, Risperidone
Low	Aripiprazole, Ziprasidone, Lurasidone

Pharmacotherapy

The first-line, evidence-based psychopharmacologic treatment of disruptive behaviors in dementia should include acetylcholinesterase inhibitors (AChEIs- to prevent confusion with Angiotensin-converting enzyme inhibitors (ACEIs)- donepezil, rivastigmine, and galantamine) and memantine. AChEIs (especially donepezil) and memantine have been shown to reduce behavioral symptoms in dementia. Since they have a more favorable safety profile than antipsychotics, they should be tried first.

TIPS FOR DEALING WITH PSYCHOTIC SYMPTOMS AND AGITATION IN OLDER ADULTS WITH DEMENTIA

Try non-pharmacologic methods first (establishing daily routines, identifying the source of agitation, etc.)

- When pharmacologic treatment is warranted, be keenly aware of the risk-benefit ratio.
- Periodically reassess the ongoing need for medications used for disruptive behaviors.
- Work with behavioral health providers, pharmacists, and social workers on a comprehensive treatment plan that includes behavioral interventions, pharmacotherapy, and working with care-givers.

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If AChEIs and memantine fail, second-generation antipsychotics that have shown efficacy in treating disruptive behaviors in dementia are the next choice. Selection of the agent should be based on side-effect profiles (Table 3), as well as the patient's comorbidities. Dosing should start low and be titrated slowly since older adults are more sensitive to side-effects. Target doses are typically lower than those used for younger patients with primary psychotic disorders (Table 4).

Antidepressants, especially SSRIs such as citalopram and sertraline, can reduce behavioral disturbances associated with dementia if there are no psychotic symptoms. They are safer than antipsychotics, but the lag time until improvement is longer. The benefits of other mood stabilizers and other psychotropic agents are currently unclear.

Table 3. Antipsychotic Pharmacologic Differences

Medication	Problems in Older Adults
Aripiprazole (Abilify)	Less α , H_1, M_1 activity, but more akathisia
Olanzapine (Zyprexa)	High H_1 (↑ sedation and metabolic side-effects) and M_1 activity (anticholinergic)
Quetiapine (Seroquel)	High H_1 and α activity (↑ risk of orthostatic hypotension)
Risperidone (Risperdal)	High α activity (↑ risk of postural hypotension), high D2 activity (↑ risk of extrapyramidal symptoms)

α =alpha; H_1=histaminergic; M_1=muscarinic; D_2=dopaminergic

Table 4. Common Medications for Dementia and Psychosis: Initial Geriatric Dose, Target Dose, Geriatric Considerations

Medications FDA-Approved for Dementia	Initial Dose	Target Dose	Geriatric Considerations
Donepezil (Aricept)	5 mg	10 mg	GI side-effects are most common (nausea, vomiting, diarrhea) and are dose-dependent. May cause weight loss, increased fatigue, or insomnia.
Galantamine (Razdyne)	8 mg	16-24 mg	GI side-effects, decreased appetite, weight loss, dizziness, headache. Take with meals and assure adequate fluid intake. Dose adjustments required in renal and hepatic impairment.
Memantine (Namenda)	5 mg	10 mg BID	Common side-effects are dizziness, headache, fatigue, constipation. Minimum of 1 week recommended before increasing dose. NTE 5 mg BID in severe renal impairment.
Rivastigmine (Exelon)	4.6 mg	9.5-13.3 mg	Dose-dependent GI side-effects are most common (nausea, vomiting, diarrhea). Monitor closely for toxicity in low weight (< 50 kg) patients. Titrate every 4 weeks.
Antipsychotic Medications			
Aripiprazole (Abilify)	2.5 mg	2.5-12.5 mg	Increased risk of akathisia which can mimic agitation, leading to further dose increases. Long half-life (72 hours), steady state not achieved for up to 2 weeks. Monitor A1c and lipids.
Olanzapine (Zyprexa)	2.5 mg	2.5-10 mg	High risk of weight gain; metabolic side-effects are dose-dependent. Monitor A1c and lipids. Dosing can be daily or split into BID-TID. Takes 6 hours to peak (oral); effects for agitation are not immediate.
Quetiapine (Seroquel)	12.5 mg	12.5-200 mg	Monitor for orthostatic hypotension and use gradual dose increases; educate patient on how to minimize risk of falls. Dosing can be daily or split into BID-TID. Monitor A1c and lipids.
Risperidone (Risperdal)	0.25 mg	0.25-1.5 mg	Monitor for orthostatic hypotension and use gradual dose increases; educate patient on how to minimize risk of falls. Dosing can be daily or split BID. Monitor A1c and lipids.
Antidepressant Medications			
Citalopram (Celexa)	10-20 mg	20-40 mg*	May cause hyponatremia. GI distress may limit adherence; may cause weight gain or loss; decreased sexual function possible. Risk of QT prolongation with doses > 20 mg/day. Escitalopram may be considered as an alternative agent.
Sertraline (Zoloft)	25 mg	50-200 mg	Less adverse effects compared to other agents; most common side-effects are GI distress, fatigue, insomnia, tremor, and sexual dysfunction

A1c=hemoglobin A1c; GI = gastrointestinal; NTE=not to exceed; *Max 20 mg/day for older adults– new recommendation

References and Resources

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