Behavior Disorders of Dementia: Recognition and Treatment

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Psychosis may pose a greater challenge than cognitive decline for patients with dementia and their caregivers. The nature and frequency of psychotic symptoms varies over the course of illness, but in most patients, these symptoms occur more often in the later stages of disease. Management of psychosis requires a comprehensive nonpharmacologic and pharmacologic approach, including an accurate assessment of symptoms, awareness of the environment in which they occur, and identification of precipitants and how they affect patients and their caregivers. Nonpharmacologic interventions include counseling the caregiver about the nonintentional nature of the psychotic features and offering coping strategies. Approaches for the patient involve behavior modification; appropriate use of sensory intervention; environmental safety; and maintenance of routines such as providing meals, exercise, and sleep on a consistent basis. Pharmacologic treatments should be governed by a "start low, go slow" philosophy; a monosequential approach is recommended, in which a single agent is titrated until the targeted behavior is reduced, side effects become intolerable, or the maximal dosage is achieved. Atypical antipsychotics have the greatest effectiveness and are best tolerated. Second-line medications include typical antipsychotics for short-term therapy; and, less often, anticonvulsants, acetylcholinesterase inhibitors, antidepressants, and anxiolytics. Goals of treatment should include symptom reduction and preservation of quality of life. (Am Fam Physician 2006;73:647-52, 653-4. Copyright © 2006 American Academy of Family Physicians.)

▶ **Patient education:** A handout on dementia, written by the authors of this article, is provided on page 653.

Virtually all patients with dementia will develop changes in behavior and personality as the disease progresses.[1] The nature and frequency of symptoms vary over the course of the illness, and psychotic features tend to present later, particularly when the patient becomes more dependent. Psychotic manifestations and other behavior problems may be more troubling and challenging than cognitive losses; these features result in an increased burden for caregivers, earlier institutionalization, and an acceleration in cognitive decline.[2]

Psychotic features of dementia include hallucinations (usually visual), delusions, and delusional misidentifications. Hallucinations are false sensory perceptions that are not simply distortions or misinterpretations. They usually are not frightening and therefore may not require treatment. Delusions are unshakable beliefs that are out of context with a person's social and cultural background. Delusional misidentification may result from a combined decline in visual function and cognition.[2] For example, patients may suspect that their family members are impostors (i.e., Capgras' syndrome), believe that strangers are living in their home, or fail to recognize their own reflection in a mirror.

In studies of patients with Alzheimer's disease,[3] psychotic features were present in 15 to 75 percent of patients. Delusional misidentifications are thought to occur in at least 30 percent of patients with dementia.[2]

Nonpsychotic behaviors associated with dementia include agitation, wandering, and aggression. Agitation represents a cluster of physical manifestations that suggest emotional distress or motor restlessness. Patients with agitation should be evaluated for an underlying precipitating cause, such as hunger, thirst, drug use (including alcohol and caffeine), or an undetected infection. Patients who display physical or verbal aggression, which often is associated with delusional misidentification, may require a combination of pharmacologic and nonpharmacologic treatments.

Nonpharmacologic Management

Nonpharmacologic interventions are important adjuncts to psychopharmacologic agents and have been proven effective in patients with dementia. These interventions

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Nonpharmacologic interventions may be used for virtually all behavior disorders in patients with dementia.	B	4, 5, 32
Atypical antipsychotics should be used as first-line agents in patients with psychotic symptoms of dementia.	A	8, 30
Divalproex (Depakote) or carbamazepine (Tegretol) should be used as second-line agents in patients with inadequate response to antipsychotic agents.	B	7, 32
The use of benzodiazepines in patients with behavior disorders associated with dementia should be limited to management of acute symptoms that are unresponsive to redirection or other agents.	C	30

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 573 or http://www.aafp.org/afpsort.xml.

may be used in most patients with dementia-related behavior disorders.[4,5]

Before introducing an intervention, the behavior problem or symptom must be identified and quantified in terms of frequency and severity. Identification and elimination of precipitating causes are essential. Goals of care should be negotiated with caregivers; the targeted behavior often cannot be eliminated completely, but it may be reduced to tolerable or acceptable levels.[6]

APPROACHES FOR THE CAREGIVER

Caregivers of patients with dementia should be educated about the disease process and the disease manifestations being exhibited. Attendance at support group meetings, personal discussion with the physician, and resources such as *The 36-Hour Day*[7] and the Alzheimer's Association (Web site: http://www.alz.org; telephone: 800-272-3900) may be helpful. In most situations, coping strategies include remaining calm and using touch, music, toys, and familiar personal items. Helping the caregiver understand the lack of intentionality of the behaviors is essential.

BEHAVIOR APPROACHES

Approaches that were helpful in the past should be tried initially. It is better to distract patients who are angry or aggressive than to try to reason with them. Asking closed-ended questions (e.g., "Would you like cereal for breakfast?") instead of open-ended questions (e.g., "What would you like for breakfast?") may be less confusing and stressful for the patient. Validation therapy focuses on responding to the emotion rather than the content of what the patient says. The use of reminiscence therapy to recount pleasurable experiences and the use of therapeutic activities such as dance, art, music, and exercise have proven to be useful. Reality orientation is not recommended except in the very early stages of the disease. When nonthreatening hallucinations or delusions are reported, reassurance to the caregiver may be the only treatment needed.

ENVIRONMENT MODIFICATION

Patients with physically nonaggressive behavior, such as pacing and wandering, may respond to the creation of a safe environment where they can walk without risk.[4] Items such as guns and knives should be removed. Making the environment safe is a work in progress; further modifications will be necessary as the disease progresses. For patients in the later stages of the disease, a safe environment may be attained only in specialized settings such as Alzheimer's units or long-term care facilities.

DEVELOPING AND MAINTAINING ROUTINES

Patients with dementia benefit from consistency. Serving meals at the same time each day reduces stress and lessens the likelihood of troublesome behaviors.

SENSORY INTERVENTION

Touch may be beneficial in many older adults who are delusional. Music therapy and pet therapy, which create a homelike environment in nursing homes, seem to lessen behaviors associated with psychosis and enhance patients' quality of life.[4]

Pharmacologic Treatment

The axioms "first do no harm" and "start low, go slow" form the cornerstone of psychopharmacologic treatment

for patients with dementia. Sequential monotherapy for a targeted behavior is recommended until improvement is achieved, side effects become intolerable, or the maximal dosage is reached. A recent systematic review[8] of studies of single-agent pharmacotherapy found that the reduction in symptoms is modest, but that small improvements may benefit the patient and caregiver. The goal of pharmacologic treatment should be reduction, not eradication, of the most troublesome behaviors. Control of symptoms in most patients will require clear identification of target behaviors (i.e., those that are most troublesome or that interfere with care), careful dosage titration, and consideration of alternate or additional agents if the behavior is inadequately controlled.

Periodic reassessment of behaviors and reprioritization of goals should be part of an ongoing management plan. Behaviors may be assessed with a caregiver interview that uses the brief version of the Behavioral Pathology in Alzheimer's Disease scale (BEHAVE-AD) or the Neuropsychiatric Inventory (NPI-Q).[9] Although the BEHAVE-AD is useful in specialty clinics, it may be cumbersome in a busy primary care practice. Family physicians should ask pertinent questions to identify problem behaviors, assess the reduction or increase in behaviors, detect changes in function, and identify the most common adverse effects of therapy. The expected effects and side effects of medication, especially the emergence of extrapyramidal dysfunction and falls, should be discussed with caregivers during every office visit. Providing caregivers with an opportunity to discuss problems by telephone may be helpful.

Several classes of drugs may be beneficial in the management of psychotic symptoms in patients with dementia *(Table 1[10-29])*. Atypical antipsychotics are the first-line agents for pharmacotherapy of psychotic symptoms.[30] Anticonvulsants and acetylcholinesterase inhibitors may be considered in patients who have an inadequate response to the initial agent.[31] Benzodiazepines may be useful for episodes of acute agitation. Systematic reviews[8,32] of these results have been published, as has a review[33] of studies of patients in long-term care.

ATYPICAL ANTIPSYCHOTICS

Atypical antipsychotics are the most thoroughly studied class of medications for patients with dementia and are the most common drugs used in clinical practice. They are better tolerated than typical neuroleptic agents, with less risk of causing extrapyramidal syndrome (EPS). In the absence of contraindications such as serious extrapyramidal dysfunction (e.g., EPS, parkinsonism), an atypical neuroleptic agent should be initiated at the lowest effective dosage and titrated weekly. Tremor, rigidity, dystonia, and dyskinesia are identified in a significant number of patients at baseline and may be exacerbated by the use of atypical antipsychotics, particularly when these agents are taken at higher dosages. Physicians must use caution when increasing dosages and observe the patient closely for the emergence of EPS. Based on the results of clinical trials,[18,26,27] there appears to be a narrow window of tolerated effective dosages. All of these agents may be administered once daily, usually at night to take advantage of their sedative effects. Two randomized controlled trials[26,27] found that risperidone (Risperdal) is effective in the management of psychotic disorders of dementia. However, a retrospective analysis of 17 placebo-controlled studies of the use of atypical antipsychotic agents to treat behavior disorders in patients with dementia found an increased mortality rate. Most deaths were from cerebrovascular events or infections. This prompted the U.S. Food and Drug Administration to issue a safety alert for all agents in this class. Quetiapine (Seroquel) is the least likely drug in this class to increase symptoms in patients with Parkinson's disease or EPS. Intramuscular administration of olanzapine (Zyprexa) has been tested in acutely agitated patients, with favorable responses compared with patients who received placebo and lorazepam (Ativan).[34] Once symptoms are acceptably controlled, the use of medications on an "as-needed" basis should be discouraged. Improvement in aberrant behavior often occurs more quickly and at lower dosages of these agents than reduction of psychotic symptoms. Although the response to medication may be modest, it has the potential for significant improvement in quality of life for patients and their caregivers.

The goal of pharmacologic treatment should be reduction, not eradication, of the most troublesome behaviors.

TYPICAL ANTIPSYCHOTICS

Although the use of haloperidol (Haldol) is discouraged in long-term care facilities, it is widely used in the management of delirium and acute agitation in other settings. Haloperidol has been used with acceptable side effects in the management of behavior disorders of dementia. If used, it should be prescribed at low dosages and for short periods (typically days), after which the patient should be switched to another agent such as an atypical antipsychotic.

A meta-analysis[35] of older trials of antipsychotic treatment for agitation in older patients with dementia

TABLE 1
Pharmacologic Agents for Management of Psychotic Disorders of Dementia

Agent	*Dosage range*	*Outcome*	*Notes*
Acetylcholinesterase inhibitors			
Donepezil (Aricept)[10,11]	10 mg at bedtime	Improvement in outpatients but not in patients in extended-care facilities	Secondary data analysis in populations studied for cognitive loss
Galantamine (Razadyne: formerly Reminyl)[12]	6 to 12 mg twice per day	Improvement on Neuropsychiatric Inventory	Secondary endpoint in populations studied for cognitive loss
Rivastigmine (Exelon)[13]	3 to 6 mg twice per day	Less anxiety and psychosis	Secondary endpoint in populations studied for cognitive loss
Anticonvulsants and mood stabilizers			
Carbamazepine (Tegretol)[14,15]	Variable	May reduce aggression	Side effects and toxicity limit use.
Divalproex (Depakote)[16,17]	375 to 1,375 mg per day	Continued improvement in agitation over time; well tolerated	—
Antidepressants			
Citalopram (Celexa)[18,19]	10 to 40 mg per day	Reduced agitation	—
Fluoxetine (Prozac)[20]	5 to 40 mg per day	—	No data for effect in nondepressed patients
Sertraline (Zoloft)[20]	25 to 200 mg per day	—	No data for effect in nondepressed patients
Trazodone (Desyrel)[14,15]	25 to 300 mg per day	Reduced verbal aggression	—
Anxiolytics			
Buspirone (BuSpar)	15 to 30 mg per day	—	No randomized clinical trials support use.
Lorazepam (Ativan)[21]	0.5 to 5 mg per day	—	No randomized clinical trials support use. Restrict use to patients with acute agitation.
Atypical antipsychotics			
Clozapine (Clozaril)[22,23]	25 to 50 mg at bedtime	Effective in reducing drug-induced psychosis in patients with Parkinson's disease	Use limited by required hematologic monitoring.
Olanzapine (Zyprexa)[24]	2.5 to 10 mg at bedtime	Improvement in agitation and aggression	Significant sedation when given at higher dosages; use with caution in patients with diabetes.
Quetiapine (Seroquel)[25]	12.5 to 300 mg at bedtime	Results in psychosis were negative.	Antipsychotic of choice in patients with parkinsonian symptoms.
Risperidone (Risperdal)[26,27]	0.5 to 1.5 mg at bedtime	Improvement in psychosis and agitation	FDA has warned about "cerebrovascular events" in patients taking this drug.
Typical antipsychotics			
Haloperidol (Haldol)[28,29]	< 1.5 mg per day	Variably effective at low dosages	Side effects limit use; not recommended except in patients with acute agitation and delirium.

FDA = U.S. Food and Drug Administration.

Information from references 10 through 29.

suggests no clear differences in clinical response. However, side effects (primarily prolonged rigidity) limit the use of haloperidol. It is one of the few drugs not implicated in the risk of falls in older adults, but this effect may be a result of marked impairment in patient mobility or its use in patients who are unresponsive to other agents.[36]

ANTICONVULSANTS

Anticonvulsant agents typically are used when psychotic behaviors result in aggressive behavior. Increasing evidence supports the use of divalproex (Depakote) or carbamazepine (Tegretol). These drugs are recommended as second-line agents in patients with inadequate response to antipsychotic agents. Multiple small, relatively

short-term trials[16,17] have proven anticonvulsants to be effective and well-tolerated. In practice, however, side effects, drug interaction, and a narrow therapeutic window may limit the use of carbamazepine. Data suggest that patients taking divalproex have continued symptomatic improvement on a stable dosage over time, although this effect may reflect the natural history of behavior disorders. Sedation is a common side effect of these agents and may limit their use. Most of the data on gabapentin (Neurontin) has been anecdotal.

ACETYLCHOLINESTERASE INHIBITORS

Acetylcholinesterase inhibitors such as donepezil (Aricept), galantamine (Razadyne: formerly Reminyl), and rivastigmine (Exelon) have been associated with a reduction in problem behaviors in patients with dementia. However, these drugs should not be considered first-line agents in the treatment of psychosis but rather adjunctive treatment. Data on primary endpoints of cognitive function in patients taking acetylcholinesterase inhibitors consistently show a delay in time to institutionalization, which may reflect improved behavior, a delay in onset of behavior symptoms, or retention of function. Although the responses are modest, even small gains or stabilization of symptoms may lower the burden for patients and their caregivers.

ANTIDEPRESSANTS

The distinction between depression with psychotic features and psychotic symptoms of dementia may be problematic, especially in patients with a history of depression or prominent negative symptoms. Small series results suggest that the use of selective serotonin reuptake inhibitors[18] and trazodone (Desyrel)[28] may be effective and could be considered in selected patients.

ANXIOLYTICS

Benzodiazepines should not be considered first-line therapy for management of chronic behavior disorders of dementia, even in patients with prominent anxiety. However, community surveys show that these drugs are commonly used in these patients.[21] No published studies support the routine use of benzodiazepines for the management of psychotic symptoms of dementia. Chronic benzodiazepine use may worsen the behavior abnormality because of the amnestic and disinhibitory effects of these drugs. In clinical practice, benzodiazepine use should be limited to management of acute symptoms that are unresponsive to redirection or other agents.[30] A short-acting benzodiazepine with prompt sedative effects may be useful to empower the caregiver or nursing facility during an episode of acute agitation that fails to respond to reassurance or removal of the precipitant. Short-acting benzodiazepines should be discontinued after the symptoms are controlled with other agents. Benzodiazepines with short half-lives, no active metabolites, and little potential for drug interaction are recommended.

In patients with intractable symptoms, hospitalization in a geriatric psychiatry unit, if available, may be necessary. Patients with Lewy body disease, who often present with hallucinations, may be particularly resistant to neuroleptics and may worsen when treated with these agents. Behavior problems are dynamic and variable and may resolve spontaneously. A reduction in dosage or elimination of agents is appropriate when target symptoms are improved. In long-term care settings, stepwise reduction in medication is more easily monitored and often will be requested by the consulting pharmacist. Although the patient's behavior may vary over time, no data support the notion that tapering medications will lead to the emergence of uncontrollable symptoms.

More research is needed on the pharmacologic management of behavior problems and psychosis associated with dementia. Community-based clinical trials with a stepwise, multiple-agent design will provide a stronger basis for recommendations and a better understanding of the impact of pharmacologic interventions in these patients.

Members of various family medicine departments develop articles for "Practical Therapeutics." This article is one in a series coordinated by the Department of Family and Geriatric Medicine at the University of Louisville School of Medicine, Louisville, Ky. Guest editor of the series is James G. O'Brien, M.D.

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