
Face to Face: Aggression in the Elderly

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The case of Mr. Johnson

Mr. Johnson is a 74-year-old retired professor whose evaluation supports a diagnosis of probable Alzheimer's disease. Treatment at this point includes an acetylcholinesterase inhibitor, as well as patient and caregiver support.

Six months later, he is becoming easily angered (Mini-Mental State [MMSE] 12/30). His anger responds well to sertraline. After another six months, the acetylcholinesterase inhibitor is discontinued due to lack of clinical benefit (MMSE 5/30). Eight months later, he is having violent episodes and tries to strangle his wife.

You assess Mr. Johnson as an inpatient. He is unable to converse, but at times can get an idea across. He makes inappropriate contact with health-care professionals. His gait and tone are normal.

Mr. Johnson responds to intramuscular haloperidol in the emergency department and later continues treatment as needed. However, his roommates still feel threatened by him. While he awaits long-term care, his wife wants to take him out on a day pass when she feels safe.

Would an atypical antipsychotic agent be a reasonable option?

In this article:

1. What is the general approach to aggression?
2. What are the treatments available?
3. What is the difference between typical and atypical antipsychotic agents?

Non-cognitive symptoms of dementia are classified as behavioural and psychiatric (BPSD). Agitated behaviour is considered inappropriate verbal, vocal, or motor activity unexplained by apparent needs or confusion.¹ Aggression is defined as "hostile actions toward others, self, or objects,"² and is often classified within the broader category of agitation.

Caregivers consider aggression the most serious problem they encounter in dementia. The consequences of aggression depend on the underlying cause, but in the demented or delirious patient, this symptom often leads to a "crisis" situation. Aside from the obvious potential for injury and added caregiver burden, aggression is often the factor in the decision to institutionalize.

Aggression presents most often in the moderate to moderately severe stages of elderly patients with Alzheimer's disease, when the patient is reliant on caregivers for basic activities of daily living.³ It

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Table 1

Causes of aggression in the elderly

- Dementia
- Delirium
- Drugs (*i.e.*, intoxication, withdrawal, interaction, *etc.*)
- Psychosis (*i.e.*, schizophrenia)
- Depression
- Personality disorder
- Pain
- Constipation
- Acute medical illness
- Unskillful caregiving style
- Environmental stressors

Table 2

Goals of therapy in the treatment of aggression

- Allow evaluation
- Eliminate risk/danger
- Improve quality of life; alleviate distress
- Optimize functional performance
- Reduce costs for patient, family, society
- Avoid institutionalization
- Reduce aggression

increases in frequency and becomes more persistent as the disease progresses. Behaviours are an early and defining symptom of frontotemporal dementia (FTD). Although people with FTD may score well on screening mental status tests, they need supervision and are

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particularly difficult to manage because of their lack of insight, disinhibition, and behaviours.

What is the general approach to aggression?

The approach to an aggressive older person depends on the severity of the aggression and the related risk to the person or to others. Ensuring a safe environment is a priority. If non-pharmacologic means are effective, then avoid pharmacotherapy. Usually, however, in cases of moderate to severe aggression, a combination of pharmacologic and non-pharmacologic approaches is recommended. If an underlying cause is identified, it can be treated specifically, but concomitant antipsychotic agents may still be beneficial if the situation continues to be potentially unsafe. Haloperidol is often the drug of choice, but there is evidence now that intramuscular olanzapine (not yet approved for use in Canada) may be an alternative.⁴

Aggression is often multifactorial, with possible underlying medical, psychiatric/neurologic, and environmental etiologies (Table 1). A person with dementia is at an increased risk of developing delirium. Therefore, when agitation or aggression present, a workup for secondary causes should be considered, rather than attributing the symptoms to dementia.

How is aggression documented?

A study designed to assess the validity and reliability of a tool to document aggression (without any other intervention) demonstrated a decline in the number of aggressive episodes from 91 at baseline to 16 at week six.⁵ Instruments to monitor aggression help caregivers to recognize, anticipate, and even avoid events.

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Table 3

Time to treat before tapering (Long-term care guidelines)

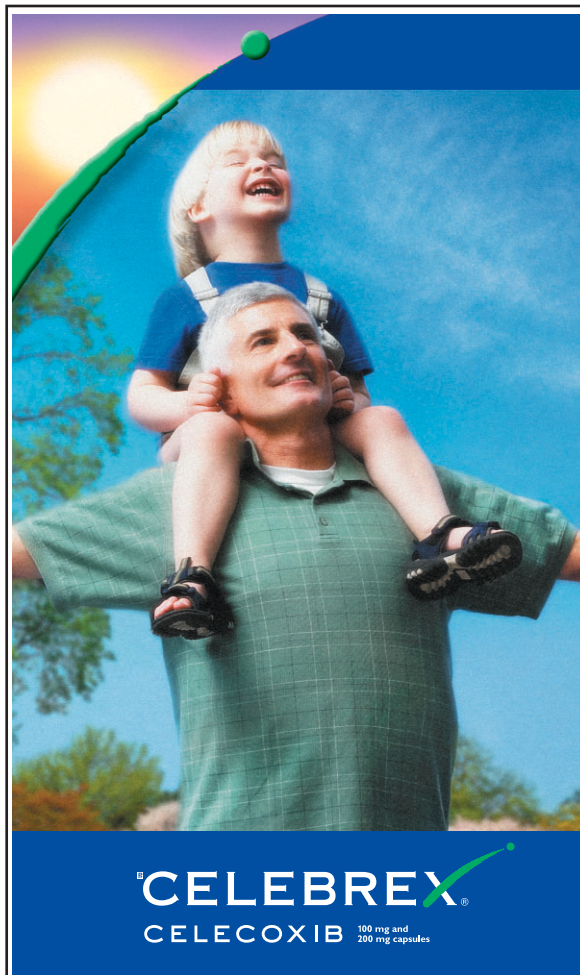
Level of agitation	Minimum treatment time	Maximum treatment time
Mild	1.5-2 months	4-6 months
Severe	2-3 months	6-8 months

There is no “gold standard” instrument for assessing aggression, however, documenting antecedents, behaviour, and consequences is recommended. Consequences may inadvertently reinforce behaviour. Behavioural monitoring charts are also recommended to assess the effects of interventions on the target symptom, to help identify adverse effects, and to document the need for continued therapy.

What treatments are available?

The 1992 joint position statement addressing psychotherapeutic agents in nursing homes developed goals of therapy for the treatment of aggression (Table 2).⁶

Verbal and physical aggression can be appropriately and effectively treated with antipsychotic medication. Screaming, inappropriate foul language, resistance to personal care, and inappropriate sexual behaviours are often better managed by non-pharmacologic means, as patients may be less



responsive to psychoactive therapies. Guidelines for use of psychoactive agents in dementia have been developed by expert consensus to avoid misuse (underuse and overuse).^{3,7,8}

An assessment period, ranging from four to seven days and up to two to four weeks, is recommended when introducing an antipsychotic drug for aggression that is not acute, as long as the medication is tolerated. During this time, evaluate effectiveness and potential adverse effects, such as orthostatic hypotension, as well as deficits in cognition, gait, and function.

There is no significant data stating when to stop medication. Experience with implementation of long-term care guidelines

suggest psychotropic medication can be effectively decreased in dosage or discontinued in approximately one-quarter to one-third of attempts (Table 3).^{8,9} After failing to taper an antipsychotic agent, it is reasonable to try again after several months. Repeated relapses

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Table 4

Considerations in prescribing a second-generation antipsychotic agent

	Clozapine	Risperidone	Olanzapine	Quetiapine
Starting dose	6.25 mg/day	0.25-5 mg/day	2.5-5 mg/day	25 mg/day
Recommended dose		0.25-2 mg/day	2.5-10 mg/day	50-300 mg/day
Preparations	Tablet	Tablet, liquid	Tablet (rapidly dissolving); IM	Tablet
EPS	None	Highest (dose-related)	Dose-related	Low
Anticholinergic effects	Highest	Lowest	Moderate	Moderate
Orthostatic hypotension	Highest; monitor cardiac patients	Low	Low/moderate	Moderate
Sedation	Highest	Lowest (about 10%)	Moderate	Moderate
Seizure threshold	Lowered	No change	No change	No change
Triglyceridemia	High	Low	Moderate/high	Low
Glucose intolerance*	High	Low	Moderate	Low
QTc prolongation	Low	Low	Low	Low
Additional comments	0.5% risks of agranulocytosis; risk of falls, delirium; swallowing problem	EPS same as conventional antipsychotics at > 2mg/day; Possible association with stroke	Associated with abnormal gait and sedation; can be given once daily	Increase in rate of accidental injuries

IM: Intramuscularly
 QTc: Q-T interval corrected for heart rate
 EPS: Extrapyramidal symptoms

*Occured only up to 60 years of age in one of several population studies. Many of the metabolic side-effects not well studied in the elderly.

suggest the need to continue the antipsychotic indefinitely. Tapering should be gradual, approximately 25% every one to two weeks.

Anticonvulsants, buspirone, selective serotonin reuptake inhibitors, trazodone, or beta blockers are other options in the treatment of aggression.

What are the typical antipsychotic agents?

A 1990 meta-analysis showed a modest advantage (18%) of typical antipsychotics over placebo for

BPSD, with symptoms including verbal and physical aggression.¹⁰ At the time, no agent was superior. Recommendations suggested that choice be made based on response and side-effect profile.

There is some evidence that the conventional antipsychotics increase the rate of cognitive decline in Alzheimer's disease and hasten mortality in Lewy body dementia (LBD).¹¹ Patients with LBD are also at increased risk of developing extrapyramidal symptoms (EPS), including neuroleptic malignant syndrome.¹² The atypical antipsychotics have lower potential for EPS, neuroleptic malignant

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syndrome, tardive dyskinesia, cognitive decline, and often, cholinergic activity.

What are the atypical antipsychotic agents?

The newer antipsychotic agents, with greater binding affinity for serotonin than dopamine receptors, are referred to in the literature as atypical, novel, or second-generation antipsychotics. Clozapine has been considered the prototype for this class, but each agent has selective binding affinities for different receptors and, therefore, unique properties.

The improved tolerability over the conventional antipsychotics is important for the elderly. The majority of the evidence and experience with these agents, however, is in a younger, schizophrenic population. The results, therefore, may not generalize to the elderly, who have a greater propensity for side-effects, more intercurrent illnesses, and often require much lower dosages of these medications. Many claims for superiority in areas other than psychosis and schizophrenia need to be validated in clinical trials. It is agreed that these medications are first-line treatments for aggression with psychosis, but consensus on aggression in any other setting has yet to be reached.

Risperidone

Risperidone has the best evidence in the elderly with aggression. In four randomized, controlled trials, elderly people with Alzheimer's, vascular dementia, and mixed dementia living in long-term care institutions were assessed for behavioural symptoms, specifically aggression.¹³⁻¹⁵ One study compared haloperidol and risperidone to placebo and found risperidone was at least as effective for

aggressive symptoms and had better tolerability. Compared with the other atypicals, risperidone is the most likely to have EPS (especially in dosages above 1 mg twice daily). It is also associated with the least propensity for weight gain and sedation.¹⁶

Safety information has been circulated by the manufacturers of risperidone pertaining to an association between this drug and cerebrovascular events in two of the four randomized, controlled trials. The number of events was small and the studies were not designed to examine this outcome, so the relationship cannot be further defined. The tri-

als with olanzapine, quetiapine, and clozapine also are not adequate to comment on any association these medications may have with stroke incidence. Stroke risk factors should be treated before choosing to initiate an atypical antipsychotic and until the association is better understood, caution should be



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Take-home message

Diagnosis

- Aggression should be investigated for a possible underlying cause.

Treatment

- Atypical antipsychotics are first-line agents for aggression in the elderly with psychosis.
- In most circumstances, trials to taper or discontinue antipsychotic medications are recommended.
- Atypical antipsychotics have a safer side-effect profile than conventional antipsychotics, but are not without serious side-effects.
- Monitoring is also an important part of intervention.

exercised in patients with cardiovascular disease.

Olanzapine

Olanzapine has also been studied in three randomized, controlled trials with elderly patients with agitation.^{4,17-19} Two studies are with patients with Alzheimer's disease and the other with patients in an acute setting using an intramuscular preparation for agitation in dementia. Compared with lorazepam (1 mg) and placebo, olanzapine (2.5 mg to 5 mg) was effective sooner (within 30 minutes) and the effect lasted longer (still significant at 24 hours) and the agent was no more sedating. There was no statistical increase in adverse events. A similar study also shows a more favourable effect in the emergency department when compared with haloperidol.^{18,19} Olanzapine is felt to have the lower risk of orthostatic hypotension than the

others in this class. It can be prescribed once daily at bedtime, while in other atypical agents, divided dosing is often recommended for a 24-hour effect. Despite a higher anticholinergic profile in in vitro studies, there was no increased risk of anticholinergic side-effects or falls at the 5 mg to 10 mg dosages in the published trials. The only risk increases were in sedation and gait disturbance.¹⁷

Quetiapine

The evidence for quetiapine in the elderly is limited to open-labelled studies that do not focus on aggression. Quetiapine has a broad therapeutic dosing range; individualization is possible. It also has less risk of motor side-effects than risperidone or olanzapine.

Quetiapine has data to support its use in Parkinson's disease and in LBD.¹⁸

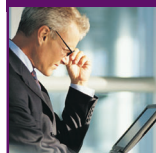
Clozapine

Although clozapine has dopamine-blocking activity, it does not cause Parkinsonism in humans and has been shown to have a beneficial effect on tremor, which is unique to this antipsychotic.¹⁸

Clozapine is the preferred antipsychotic agent in elderly patients with Parkinson's disease. However, in general, the other agents are preferred for elderly without Parkinsonism because clozapine has relatively higher rates of anticholinergic effects, sedation, and orthostatic hypotension. Table 4 summarizes some of the considerations in prescribing a second-generation antipsychotic agent.

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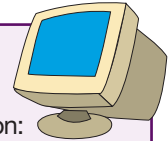
What is the goal of therapy?

Consensus guidelines and experience suggest a role for atypical antipsychotic medications in aggressive older people. Evidence supporting the use of atypical antipsychotic medications for aggression in the elderly is still limited. The goals of therapy could be measured not only in the context of controlling behaviour, but on effects of caregiver burden, quality of life, and delaying institutionalization. 

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