UNIVERSITY OF CALGARY
FACULTY OF MEDICINE

Getting Aggressive with Dementia

Adrienne Cohen, MD, BSc, FRCPC
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Up to 90% of people with dementia experience behavioural symptoms and 25% to 30% are aggressive during the course of their illness.[1] However, new onset of aggression should not be attributed to dementia without further assessment.

The differential diagnosis of aggression in the elderly is listed in Table 1.[1] Diagnoses should be confirmed if aggression is new, changing, or not responding to interventions.

Although dementia is defined by cognitive changes with functional impact,[2] behavioural and psychiatric symptoms of dementia (BPSD) are at least as important. Caregivers name aggression as the most serious symptom of dementia,[3] but it should not be considered an inevitable or untreatable part of the dementia process. Caregiving strategies (*i.e.*, reassurance, routine, redirection,[4] and reorientation) should be discussed, as they may help avoid some of the environmental triggers for aggression.

Mr. Furley's aggression

Mr. Furley, 83, presents to your office with aggression. He was admitted to hospital with a hip fracture following an unwitnessed fall 2 weeks earlier. He is agitated and he hits and bites nurses, mostly in the evening.

Mr. Furley is incontinent. He can be prompted to void, but will not call for nurses. His examination reveals:

- 13/30 perseverative field
- Urine e-coli > 108
- Hemoglobin: 115 g/L
- Mean cell volume: 95 femtolitres

His examination is also notable for hip scar and bruising of the knees.

Corroborative history was unavailable for over a week.

For a followup on Mr. Furley, see page 151.

How do I choose the appropriate therapy?

The literature and evidence can guide our approach to aggression in dementia (Table 2).

First, consider the goals of therapy in the treatment of aggression, which include:

- eliminating risk and danger,
- improving quality of life,
- alleviating distress,
- allowing evaluation,
- optimizing function,
- avoiding institutionalization, and
- reducing costs to patient, family, and society.[5]

Elimination or control of aggressive behaviour is secondary.

In one study, monitoring behaviours successfully decreased the number of aggressive events identified from 91 to 16 over six weeks.[6] Charting the ABCs of aggression (antecedents, behaviours, and consequences)[7] may identify precipitants and consequences that reinforce or deter behaviours. The medical work-up and monitoring can thus help identify underlying causes, which we can specifically address. Then, optimization of all possible contributing factors and comorbidities, and ongoing monitoring, can improve the chances of successful management.

Table 1

Differential diagnoses of agitation in the elderly

Diagnosis	Comment
• Dementia	Most common cause of aggression in older people
• Delirium	*E.g.:* Pain, acute medical disturbances and illnesses, drugs, urinary retention, fecal impaction
• Drugs/alcohol	Interaction, withdrawal, intoxication
• Psychiatric	
• Personality disorder/ disruptive traits	
• Environmental stressors	*E.g.:* Sundowning, catastrophic reaction, unskillful caregiving

Should I use medication?

Psychosocial and environmental interventions should form the basis of management wherever possible. Pharmacologic treatment is often considered in potentially dangerous situations or when other management fails. Combination therapy is also indicated in many instances of moderate to severe aggression.

Overmedication is a frequent consequence of aggression;[1] therefore, there should be clear indications for drugs, and

Dr. Cohen is an assistant professor of medicine, University of Calgary, and a physician, department of geriatric medicine, Foothills Medical Centre, Calgary, Alberta.

Table 2

General approach of aggression in dementia

- History/corroborative history and physical
- Medication review/substance use
- Directed investigations to assess potential causes of delirium/pain/psychosis
- Recording and monitoring
- Interventions:
  - Directed and non-targeted
    - Psychosocial—appropriate setting: home, facility, specialized units; education; support; lighting, music, *etc.*
    - ± Pharmacologic
  - Ongoing monitoring, recording, re-evaluation
  - Referral/consultation

Table 3

Medications for aggression in dementia

Medication	Starting dosage	Recommended dosage	Comments/adverse effects
Donepezil	5 mg/day	10 mg/day	GI S/E; sleep disturbance; caution if asthma; COPD; CV conduction disturbance; epilepsy
Rivastigmine	1.5 mg bid	3-6 mg bid	GI S/E; good evidence in LBD; caution as per donepezil; less potential for drug interactions or sleep disturbance
Galantamine	4 mg bid	8-12 mg bid	As per donepezil
Haloperidol	0.5 mg/day	1-3 mg/day	Multiple routes of administration; high EPS; relatively safe cardiac profile; monitor QT
Risperidone	0.25-0.5 mg/day	0.25-2 mg/day (bid)	Dose-dependent EPS and orthostatic hypotension; approved for BPSD in Canada; least propensity for weight gain and sedation of the atypicals
Olanzapine	2.5-5.0 mg/day	2.5-10 mg/day	S/E (abnormal gait and sedation); in vitro, highly anticholinergic; higher rate of obesity, glucose intolerance, and elevated TG
Quetiapine	12.5-25 mg/day	50-300 mg/day (bid)	No RCT in dementia; preferred antipsychotic for Parkinson's disease; low EPS; moderate sedation; broad therapeutic range
Carbamazepine	50-100 mg bid	100-1,000 mg/day (bid); levels 5-8 g/L	Ataxia; sedation; drug interactions; orthostasis and dizziness; monitor CBC, LFT for serious S/E

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documentation of whether goals are specifically achieved (versus sedation/chemical restraint) without significant adverse effects.

Medications should be minimized and the adage "start low, go slow" is paramount (Table 3). In certain cases, it may be reasonable to accept a partial response.

Which medication do I choose?

Expert consensus has been difficult to reach on "the best" medication for aggression in a given situation. In recently published guidelines for treatment of behavioural symptoms in long-term care, consensus could only be reached for the drug to use in aggression with psychosis (*i.e.*, neuroleptics).[8] The American Academy of Neurology[6] recom-

mended use of the atypical antipsychotics as first-line agents for aggression in dementia. Meta-analyses have shown a modest benefit of conventional antipsychotics in aggression in dementia.[9] The atypical antipsychotics are generally felt to be safer and effective.

Other considerations include the type of dementia, risk for falls, seizure history, metabolic and cardiovascular risk, as well as timing of agitation and need for sedation.

Prevention

There is increasing evidence that acetylcholinesterase antipsychotics may prevent or delay onset of aggressive behaviours in Alzheimer's disease (AD) or mixed dementias over the long term. Currently, rivastigmine has the best data for a clinically significant effect on behaviour; its use may be associated with a need for fewer psychotropic agents.[10]

Urgency

Benzodiazepines, antipsychotics, and the combination of the two have been studied in aggression in an acute emergency. Haloperidol is easily administered and acts quickly. It is less sedating than lorazepam, which is the benzodiazepine most often used in urgent, aggressive situations. In three published randomized controlled trials, intramuscular olanzapine compared favourably with haloperidol[11,12] and lorazepam[13] for emergency cases of aggression.

Associated psychiatric symptoms

Aggression may be associated with other manifestations of BPSD, including psychosis. There is consensus that the atypical neuroleptics are the preferred medications in the case of psychosis.[8,14] Dementia and depression are also associated. In more advanced dementia, depressed mood cannot be well communicated and may be expressed as aggressive behaviour. Antidepressants are worth a trial if depression is felt to be underlying a person's misconduct. Recent studies with selective serotonin reuptake

Table 3

Medications for aggression in dementia (cont'd)

Medication	Starting dosage	Recommended dosage	Comments/adverse effects
Divalproex	125 mg qhs	500-2,500 mg; levels ~50 mg/L	Less sedation, ataxia, and drug interactions compared with carbamazepine; GI S/E; monitor CBC, liver, and, if needed, INR for serious S/E
Gabapentin	100 mg daily or bid	300-2,400 mg (divided)	Sedation; adjust for creatinine clearance
Citalopram	10 mg/day	10-40 mg/day	GI S/E; sexual dysfunction; tremor
Sertraline	25 mg/day	25-150 mg/day	As per citalopram
Paroxetine	5-10 mg/day	10-30 mg/day	As per citalopram; more sedating; more P450 interaction; more anticholinergic; both potentially good for anxiety, panic
Trazodone	25-50 mg/day	50-300 mg/day	Sedation; postural hypotension; priapism; caution in cardiac disease
Buspirone	5 mg tid	15-60 mg/day (tid)	S/E generally mild; 2-4 weeks for effect
Lorazepam	0.5 mg	0.5–2 mg	Withdrawal; dependence; sedation; confusion; falls; paradoxical agitation
Oxazepam	7.5-15 mg	7.5-45 mg	As per lorazepam
Propanolol		10-240 mg	Hypotension; bradycardia; COPD exacerbation; worsen hypoglycemia and cognition
Pindolol		10-60 mg	As per propanolol

GI: Gastrointestinal
S/E: Side-effects
COPD: Chronic obstructive pulmonary disease
CV: Cardiovascular
bid: Twice daily
LBD: Lewy body dementia
RCT: Randomized controlled trial
TG: Triglyceride
EPS: Extrapyramidal side-effects
CBC: Complete blood count
LFT: Liver function test
qhs: Every hour of sleep
INR: International normalized ratio
tid: Three times daily
BPSD: Behavioural and psychiatric symptoms of dementia

inhibitors[15-17] have demonstrated some benefit on emotional and behavioural symptoms in non-depressed, demented people.

Financial considerations

Budgets are a concern for the individual, institutions, and society. The newer agents generally are more expensive. Price differentials exist within medication classes. There are direct and indirect cost savings associated with treatment of aggression in this population.

How long do I continue therapy?

Medications may be administered during an acute aggressive episode without the need for ongoing use. For more prolonged therapy, and if there are no limiting adverse effects, psychotropics should be continued for an assessment period of four days to four weeks.[15] Medication may be discontinued for inadequate response or clinically significant side-effects. If the drug is tolerated and effective, there are no data on how long to continue. U.S. guidelines recommend attempts to taper and discontinue these agents at least once to twice a year,[8,14] unless there are repeated relapses, suggesting the need to continue the treatment indefinitely. It is recommended that the dosage of antipsychotics be decreased by 25% every one to two weeks.[14] CME

What happened to Mr. Furley?

Mr. Furley's nurses' initial request was to help his nighttime behaviour. He had a trial of trazodone, up to 125 mg in the evenings. The medication sedated Mr. Furley for up to 4 hours, after which he would hit and bite the staff, and require security.

In the interim, investigations were repeated, as he resisted care during the day, not allowing any toileting or diaper change. A trial of daytime risperidone was not successful. Corroborative history from Mr. Furley's daughter revealed that he had not been physically aggressive in the past.

Mr. Furley responded to a trial of quetiapine, 50 mg for two nights. On the third night, prior to transfer to a continuing care unit, he became aggressive again. The sundowning was better controlled with an atypical neuroleptic. The resistance to care was managed by nursing approach. When the nurses approached Mr. Furley, he immediately acquiesced and was co-operative.

Take-home message

- Charting the ABCs (antecedents, behaviours, and consequences) may identify precipitants and consequences that may reinforce or deter behaviours.
- The optimization of all contributing factors, and comorbidities, as well as ongoing monitoring, can improve the chances of successful management.
- In more advanced dementia, depressed mood cannot be well communicated, and may be expressed as aggressive behaviour.
- It is recommended that the dosage of antipsychotics be decreased by 25% every one to two weeks.

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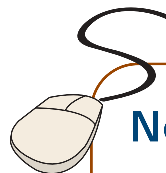
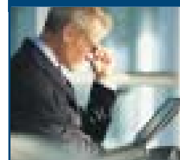


Net Readings

1. Alzheimer's Association
   www.alz.org
2. Alzheimer's Disease Education and Referral Centre
   www.alzheimers.org
3. Expert Consensus Guideline Series
   www.psychguides.com

www.stacommunications.com



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