CME

Approach to managing behavioural disturbances in dementia

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ABSTRACT

OBJECTIVE To review practical evidence-based treatment of behavioural symptoms in dementia.

SOURCES OF INFORMATION MEDLINE was searched from January 1966 to December 2004 and PsycINFO from January 1967 to December 2004 using the key words "BPSD" (behavioural and psychological symptoms of dementia) and "behavioral disturbances dementia." I also reviewed the bibliographies of recent review papers and original articles.

MAIN MESSAGE Family physicians who manage hospital inpatients and care for people in nursing homes are asked to prescribe medications for demented patients. This review discusses alternatives to drugs, indications for appropriate use of drugs, frequently encountered side effects of drugs, and considerations for those with neuroleptic sensitivity. I suggest an approach that employs a combination of behavioural, environmental, and pharmacologic interventions to address disruptive behaviour in patients with dementia.

CONCLUSION Optimal treatment of behavioural disturbances in patients with dementia involves nonpharmacologic approaches and using medications with demonstrated efficacy. Pharmacologic treatment should target only those symptoms or behaviours that respond to medication. This approach minimizes unnecessary medication use and reduces adverse outcomes.

RÉSUMÉ

OBJECTIF À partir de données probantes, proposer un traitement des troubles comportementaux rencontrés dans la démence.

SOURCES DE L'INFORMATION MEDLINE a été consulté (de janvier 1966 à décembre 2004) de même que PsycINFO (de janvier 1967 à décembre 2004) à l'aide des mots-clés *BPSD (behavioural and psychological symptoms of dementia)* et « *behavioural disturbances dementia* ». L'auteur a aussi relevé les bibliographies d'articles de revue et d'articles originaux récents.

PRINCIPAL MESSAGE Le médecin de famille qui exerce en milieu hospitalier ou en centre d'hébergement est souvent appelé à prescrire des médicaments pour les patients atteints de démence. Cette étude traite des mesures non pharmacologiques, des médicaments les plus appropriés et des effets pharmacologiques indésirables les plus fréquents, et souligne la nécessité de tenir compte de la sensibilité particulière de certains patients aux neuroleptiques. L'approche suggérée comprend des interventions d'ordre comportemental et environnemental et des mesures pharmacologiques pour corriger les troubles comportementaux perturbateurs.

CONCLUSION Le traitement optimal des troubles comportementaux chez les patients atteints de démence s'appuie sur des médicaments dont l'efficacité est établie, mais aussi sur une approche non pharmacologique. Les médicaments choisis devraient viser uniquement les symptômes ou comportements qu'ils peuvent corriger. Cette approche permet de réduire la médication inutile au minimum, en plus de réduire les effets indésirables.

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Case description

You are called about an agitated 76-year-old man, Mr L.B., who was recently admitted to the care facility complaining of seeing people coming into his room. The nurse reports he is also resistive (physically resists cooperating) and strikes out during care. An as-needed haloperidol order had been obtained from the doctor on call, but Mr L.B. developed marked extrapyramidal symptoms after several doses. What conditions could explain his behaviour and how would you intervene?

The number of elderly people in Canada, especially those older than 85, is expected to increase dramatically during the next 30 years.[1] In 1994, people older than 65 made up 11.6% of the population; by 2016, they are expected to make up 16%, and by 2041, 23%.[1] An estimated 592 000 Canadians will be affected by dementia by the year 2021,[1] and many of these people will exhibit behavioural disturbances.[2]

A study by Bronskill et al[3] showed that 24% of patients who had not used neuroleptics recently were treated with antipsychotic drugs during the first year of admission to Ontario nursing homes. Controversy has emerged recently regarding use of atypical antipsychotics in dementia, due to concerns about risk of stroke.[4,5] There is also increasing recognition of Lewy body dementia (LBD) and growing awareness of the need for caution in treating these elderly patients.

Sources of information

MEDLINE and PsycInfo databases were searched using the key words "BPSD" (behavioural and psychological symptoms of dementia) and "behavioral disturbances dementia." Recent articles and bibliographies were also searched. Several review articles and published randomized controlled trials (RCTs) were found. These RCTs established the efficacy and tolerability of atypical antipsychotics and provided level I evidence supporting their use. Antidepressants and anticonvulsants are supported by less robust evidence, but do have RCTs demonstrating their efficacy for BPSD.

In 1990, Schneider et al did a meta-analysis of 33 published reports on use of antipsychotics for dementia.[6] In this analysis, placebo response rates varied from 0 to 67%, and antipsychotics as a class had only a modest benefit. The derived treatment effect size was estimated at 18% (ie, only 18% of patients had better results with neuroleptics than with placebo). Defilippi and Crismon, after reviewing studies of antipsychotic agents in dementia, concluded that risperidone could be considered a first-line agent and proposed an algorithm for treatment of BPSD.[7]

In 2002, Conn reviewed the literature on management of psychosis and aggression in dementia to examine the evidence for each class of medication.[8] The best evidence supported antipsychotics. Antidepressants (trazodone and citalopram) and carbamazepine also had evidence of efficacy, and acetylcholinesterase inhibitors (AChEI) were seen as warranting further study. The Canadian Coordinating Office for Health Technology Assessment reviewed use of novel antipsychotics in March 2003 and found seven RCTs of satisfactory quality that demonstrated the efficacy of risperidone and olanzapine for BPSD.[9]

Approach to BPSD

Various symptom clusters can arise in the course of dementia (**Table 1**). As behavioural manifestations of dementia respond modestly to pharmacotherapy, it is important to identify and treat reversible conditions that present with similar symptoms, such as medical and psychiatric illnesses, drug toxicity,

Table 1. Disruptive symptom clusters in dementia

Agitation (pacing, wandering, restlessness, inability to sit long enough to eat)
Aggression (verbal and physical, which might target staff or other residents)
Physical resistance and noncompliance with care
Abnormal vocalizations (screaming, shouting)
Psychosis (hallucinations, delusions)
Depressive symptoms (apathy, disinterest)
Sexual behaviours (verbal comments, masturbation, grabbing staff)
Sleep disturbances (day-night reversal, getting up to dress)

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and delirium (**Table 2**). All guidelines stress that initial interventions should be nonpharmacologic. Generally, this means beginning with environmental and behavioural modifications.

Table 2. Things to consider when faced with an agitated demented patient

Review possible physical causes (pain, infection)
Examine his or her medication list (especially for anticholinergic drugs)
Look for contributing environmental factors (eg, noise associated with shift change)
Consider psychiatric diagnoses (depression, anxiety)
Focus on one target behaviour to address
Reserve medications for situations where the safety or well-being of the patient or others is at risk

Behavioural and environmental approaches

Using behavioural interventions first might provide staff with a sense of control of the situation and reduce unrealistic expectations of immediate results. Often, the process of documentation gives insight into what triggers disturbed behaviour and indicates ways of avoiding the problem. Behavioural mapping might also affect staff members' perception of how frequently the behaviour occurs, how severe it is, and how much it can be managed.

Charting using the **A**ntecedents-**B**ehaviour-**C**onsequence method can help to identify temporal patterns and precipitating events (**Figure 1**[10]). After data are collected, the chart could indicate an activity, such as bathing; an approach issue, such as sex of the caregiver; or a time of day, often the evening, that suggest a need for intervention before the behaviour occurs.

Studies looking at the value of nonpharmacologic approaches have found some efficacy for behavioural and environmental interventions.[11-13] Activity programs, music, behaviour therapy, light therapy, caregiver education, and environmental changes have all been shown to have some benefit.[14] Behaviour management techniques were shown to be as effective as trazodone or haloperidol for agitation in patients with Alzheimer-type dementia.[15] Where practical, the approaches listed in **Table 3** can be tried.

Figure 1. Antecedent-Behaviour-Consequence charting template

DATE AND TIME OF DAY	ANTECEDENT (IS THERE A TRIGGER?)	BEHAVIOUR (DESCRIPTION)	CONSEQUENCE (WHAT WAS THE RESPONSE?)

Adapted from Proulx.[10]

Table 3. Behavioural and environmental interventions

Reduce environmental overstimulation
Consider physical interventions
Put up bright visual barriers or STOP signs to help prevent patients entering rooms uninvited
Use written cues to help reduce repetitive questioning
Examine the patient "mix" on the ward. Are there screamers? Room-enterers?
See whether a change of room-mate reduces altercations
Note whether behaviour is inappropriate only *for the setting* Provide areas for "problem" behaviours (eg, wandering, masturbating)
Minimize catastrophic reactions by advising staff to:
• use a gentle tone of voice (speak low and slowly)
• gesture and point
• employ one-step instructions
• use a 5-second delay between a verbal prompt and physical assistance
• leave and approach again (as necessary) at 30-minute intervals
Use exercise and structured activities to help reduce purposeless motor activity
Where local resources exist, get outreach teams to assist with making care plans, suggesting specific behavioural interventions, and educating staff

Pharmacotherapeutic approaches

Avorn and Gurwitz[16] advise that, before starting a medication for a nursing home resident, certain questions should be asked (**Table 4**[16]). Some behaviours respond poorly to medications (**Table 5**), and even when behaviours are responsive, drugs can take several weeks to have their full effect. Studies involving medication for BPSD suggest there is a fairly narrow dose range above which efficacy does not increase, and side effects do (**Table 6**).[17-19]

Choice of medication. Where possible, medication should be tailored to presentation. This involves targeting depressive symptoms, psychotic features, or manic behaviour with specific drug therapy. In practice, a series of medication trials might be needed before arriving at a suitable treatment. Challenges for clinicians include remaining patient, changing only one intervention at a time, and treating for long enough to allow for a therapeutic response. My recommendation is to limit psychotropic drugs to no more than three (and preferably two), as it is otherwise difficult to know which medication is the agent of change. Similarly, as-needed doses of medication should be minimized in favour of small, scheduled doses.

Using criteria from the Canadian Task Force on Preventive Health Care,[20] the antipsychotics risperidone and olanzapine, the mood-stabilizing anticonvulsants carbamazepine and valproic acid, and the antidepressants citalopram and trazodone have level I evidence supporting their use. Studies on nonneuroleptics have smaller patient numbers, but each nonneuroleptic drug has at least one RCT with positive results for treating BPSD.

Table 4. Questions to ask before starting a drug

What is the target problem being treated?
Is the drug necessary?
Are nonpharmacologic therapies available?
Is this the lowest practical dose?
Could discontinuing medication help to reduce symptoms?
Does this drug have adverse effects that are more likely to occur in older patients?
Is this the most cost-effective choice?
By what criteria, and at what time, will the effects of therapy be assessed?

Data from Avorn and Gurwitz.[16]

Table 5. Behaviours that respond poorly to drugs

Wandering
Pacing
Entering rooms uninvited
Attempting to leave
Making disruptive vocalizations
Voiding inappropriately

Table 6. Medications that have demonstrated efficacy for behavioural and psychological symptoms associated with dementia

DRUG	DAILY DOSAGE (MG)	SIDE EFFECTS
Risperidone	Start 0.25 Therapeutic 1.0 Maximum 2.0	Postural hypotension
Olanzapine	Start 2.5-5.0 Therapeutic 5.0 Maximum 10.0	Hyperglycemia, weight gain
Citalopram	Start 10.0 Therapeutic up to 30.0	Hyponatremia, increased risk of gastrointestinal bleeding if anticoagulant also administered
Trazodone	Start 25.0-50.0 (given in twice daily doses of 12.5-25.0) Maximum 200.0	Postural hypotension, priapism (rare), sedation

Antipsychotics. In recent years, antipsychotics have been seen as first-line treatments. Published guidelines, including those from the Canadian Consensus Conference on Dementia, recommend antipsychotics following implementation of environmental measures.[21-23] Of the four available atypical antipsychotics, only risperidone is currently approved in Canada for management of behavioural disturbances in patients with dementia.

Several studies in nursing home patients concluded that about 1 mg/d of risperidone was optimal for balancing efficacy and side effects.[17,18,24] Street et al[19] showed efficacy for olanzapine at 5-mg and 10-mg daily doses; the lower dose was most effective. A recent study was less conclusive, as all groups (including the placebo group) showed improvement in the primary outcome measure.[25] Open-label studies have shown quetiapine to be well tolerated by patients with Parkinson disease and by those sensitive to neuroleptics.[26,27] A National Institute of Mental Health study, the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), is under way comparing risperidone, olanzapine, quetiapine, citalopram, and placebo in dementia patients with psychotic features or agitation. Results of this 36-week RCT are expected in 2006.[9]

Warnings have been issued recently regarding an apparently increased risk of cerebrovascular adverse events seen in RCTs of both risperidone and olanzapine.[4,5] A recent analysis concluded, however, that there was no evidence that risk of stroke associated with use of risperidone or olanzapine increased over risk associated with typical antipsychotics for the elderly.[28]

As we await additional clarification of the extent of increased risk, obtaining informed consent and frank discussion with family (or substitute decision makers) is warranted. In general, following principles of best practice involves advocating for patients and reserving pharmacologic treatment (of any type) for behaviours that put patients, staff, or others at risk. Choosing to use medication involves weighing potential risks and benefits, while keeping safety, quality of life, and dignity in perspective. Some patients with dementia might not receive basic care because of their disturbed behaviour; judicious use of pharmacologic agents might allow them to receive this care.

Antidepressants. Trazodone has been shown in several studies to have beneficial effects on disruptive behaviour in dementia.[14,29] Citalopram was shown to be more effective than perphenazine or placebo in a 17-day study of hospitalized inpatients with behavioural disturbances.[30] Because selective serotonin reuptake inhibitors (SSRIs) can cause transient, but occasionally persisting, hyponatremia,[31] serum sodium levels should be checked periodically, especially in patients with low-normal sodium levels at baseline. There is also evidence of greatly increased risk of gastrointestinal bleeding among those taking SSRIs and concurrent anticoagulant therapy.[32]

Mood stabilizers. Carbamazepine has been shown to be effective for BPSD,[33] but its numerous side effects limit its usefulness for elderly people. A recent discussion of available nonneuroleptic options concluded that, while carbamazepine was demonstrably effective, it had not been widely used due to concerns about toxicity and drug interactions.[34] Several open-label studies[35,36] and a placebo-controlled study[37] have demonstated efficacy for sodium valproate, but a review by the Cochrane Collaboration recently concluded that there was insufficient evidence to recommend it for agitation in dementia.[38]

Acetylcholinesterase inhibitors. A recent meta-analysis concluded that AChEIs have a modest benefit for neuropsychiatric symptoms in Alzheimer disease.[39] A prospective placebo-controlled study showed that galantamine was effective in *preventing* the emergence of behavioural disturbances in *asymptomatic* Alzheimer patients[40]; AChEIs might have an increasing role in the future for BPSD in LBD where antipsychotics are less helpful. There is evidence of efficacy of rivastigmine in LBD for treatment of delusions, hallucinations, and behavioural problems.[41] For frontotemporal dementia, results with AChEI therapy have been mixed,[42-44] but SSRIs have been recommended for this condition. In one study, however, paroxetine was not shown to be of benefit.[45]

Hormonal treatments. People with dementia sometimes exhibit inappropriate sexual behaviour. Some

behaviour, such as disrobing and public masturbation, does not always require medication because it is inappropriate only for the setting. When staff or other residents are at risk from a patient's sexual aggression, a treatment approach including SSRIs, antipsychotic medication, and hormonal agents has been suggested.[46] There are no controlled studies of this treatment, and informed consent is required because many treatments are off-label.

Drugs to avoid

Typical low-potency antipsychotics (eg, chlorpromazine, thioridazine, methotrimeprazine) and tertiary amine tricyclics (amitriptyline, imipramine) are more likely to cause orthostatic hypotension or anticholinergic effects. Typical high-potency antipsychotics, such as haloperidol, might have a role in short-term treatment. A Cochrane review concluded that, while there was evidence for using haloperidol to control aggression, its routine use for agitation in dementia could not be recommended.[47]

Anticholinergic drugs (eg, benztropine, procyclidine) might worsen cognition and increase the likelihood of delirium. If drugs are required to control extrapyramidal symptoms, I suggest using different medications.

Benzodiazepines are usually not first-line treatment. Their use might be justified on a short-term basis for intractable anxiety or sleep disruption. They could also be used before care is provided. Lorazepam and oxazepam lack active metabolites and are less likely to cause accumulation or hangover. Zopiclone is generally well tolerated for treatment of sleep disturbances.

Side effects of medications

Increased risk of falls. Nearly all psychotropic medications can impair gait. Falls are thought to be partly a function of a drug's effect on balance, sedative properties, potential for orthostatic hypotension, and extrapyramidal effects. The original risperidone studies did not show an increased risk of falls (compared with placebo) at drug doses of ≤1.0 mg/d.[17,18] A 1998 study of nursing home patients showed SSRIs and tricyclic antidepressants had similar associated risk of falls.[48] Benzodiazepines have been associated with an increased rate of falls and a 1.47 increased risk of hip fractures (at doses equivalent to ≥3 mg of diazepam daily).[49] More recent work has shown that antidepressants increased hip fracture rates in community-living elderly women by a factor of 1.7; no increased risk was seen with benzodiazepines.[50]

Tardive dyskinesia. Patients with dementia, who have diminished physiologic and cognitive reserves, could be at greater risk of oral-buccal-lingual, limb, and trunk movements. The literature shows a high risk of tardive dyskinesia in elderly people taking typical antipsychotics (63.1% at 33 months of treatment).[51] This contrasts with atypical antipsychotics, such as risperidone, olanzapine, and quetiapine, which are associated with tardive dyskinesia rates of 2.5% to 3% at 1 year.[51-53]

Metabolic side effects. Altered lipid metabolism and impaired glucose tolerance have been associated with treatment using atypical antipsychotics. A 2002 study of patients with schizophrenia showed an increased risk of diabetes with olanzapine treatment.[54] It is advisable to follow blood sugar levels closely and to consider alternative therapy when patients are known to have diabetes.

Neuroleptic-sensitive populations. Antipsychotic medications can be risky for patients with features of LBD (**Table 7**[55]). Caution is required when treating psychotic features in patients with Parkinson disease or a history of neuroleptic malignant syndrome (a serious life-threatening syndrome associated with fever, autonomic nervous system disturbances, and increased creatine phosphokinase).

Table 7. Consensus criteria for Lewy body dementia

Progressive cognitive decline sufficient to interfere with normal social or occupational function
Probable Lewy body dementia requires two, and possible Lewy body dementia requires one, of the following: • Fluctuating cognition • Recurrent visual hallucinations • Spontaneous motor features of parkinsonism
Supportive features • Falls • Syncope • Sensitivity to neuroleptics • Systematized delusions • Hallucinations in other modalities

Adapted from McKeith et al.[55]

Case wrap-up

In our case, Mr L.B. has features consistent with LBD, so antipsychotic medication should not be first-line therapy. Formed hallucinations might be exacerbated by visual impairment and might respond to better lighting, improved contrast, removal of clutter, and optimal stimulation of remaining intact senses. For troubling visual hallucinations, an AChEI might be helpful.[56] When patients act on their hallucinations or become delusional and aggressive, quetiapine might be the preferred agent (50 to 100 mg/d).

Conclusion

It is important to make a diagnosis and rule out treatable conditions. The target behaviour must be clear. Environmental and behavioural interventions should be considered first; after these, trials of medications with a favourable balance of risks and benefits could be initiated. If these measures are not helpful, referral to an outreach team, a geriatric psychiatrist, or a geriatrician should be considered.

Postscript

After this article was submitted, several important developments occurred. The United Kingdom's Committee on Safety of Medicines advised physicians to avoid using atypical antipsychotic medications for behavioural disturbances in dementia and to consider withdrawing them from patients currently taking them.[57] In the United States, the Food and Drug Administration issued a warning reminding doctors that these drugs were not approved in the United States for use in elderly patients with dementia and advising mortality associated with their use doubled.[58]

Several recently published studies have addressed treatment of behavioural disturbances in dementia. Rates of falls[59] and tardive dyskinesia[60] were similar for both novel antipsychotics and older medications. Higher doses of newer medications have demonstrated a risk of extrapyramidal side effects similar to the risk demonstrated by older drugs.[61] The risk of cerebrovasuclar events seems to be similar for atypical and typical antipsychotics, suggesting that antipsychotics should not be chosen based on risk of stroke.[62] Quetiapine was not found to be superior to placebo in BPSD and showed an adverse effect on Mini-Mental State Examination scores.[63] A review by the Cochrane Collaboration concluded that there was insufficient evidence to recommend trazondone for use in BPSD.[64] A yet-to-be-released review by the Cochrane Collaboration is expected to conclude that there is evidence for efficacy of risperidone in aggression but not for other target behaviour in dementia, similar to the conclusion regarding haloperidol.[65] An article published in the *Journal of the American Medical Association*

EDITOR'S KEY POINTS

- Behavioural symptoms are not infrequently encountered in dementia, and family doctors are usually asked to manage them.
- Given the modest potential for improvement with medications, all guidelines emphasize that initial management should be environmental and behavioural.
- Assessment includes checking for physical causes, reviewing medication lists, noting environmental changes, considering psychiatric diagnoses, focusing on one behaviour to address, and reserving medications for cases where patient or staff safety is at risk.
- Atypical antipsychotics are considered first-line choices. Antidepressants are helpful in disruptive behaviour; mood stabilizers, acetylcholinesterase inhibitors, and hormonal treatments are considered secondary medications. Medication choice should target specific behaviours, be given at the lowest effective dose, and have benefits that clearly outweigh potential side effects.

POINTS DE REPÈRE DU RÉDACTEUR

- Les symptômes d'ordre comportemental sont assez fréquents dans la démence et c'est généralement le médecin de famille qui est appelé à les traiter.
- Comme le potentiel de la médication pour corriger ces troubles est relativement limité, les directives de pratique insistent toutes pour dire que l'approche initiale devrait être environnementale et comportementale.
- Dans l'évaluation, on doit rechercher les causes physiques, vérifier la médication, noter les changements environnementaux, tenir compte du diagnostic psychiatrique, mettre l'accent sur un comportement donné et réserver la médication pour les cas où il y a menace pour la sécurité du patient ou du personnel.
- Les antipsychotiques atypiques sont considérés comme des premiers choix. Les antidépresseurs sont utiles en cas de comportement perturbateur; les régulateurs de l'humeur, les inhibiteurs de l'acétylcholinestérase et les traitements hormonaux sont des choix de seconde intention. La médication devrait viser un comportement spécifique, être administrée à la plus petite dose efficace et comporter des avantages nettement supérieurs à leurs effets indésirables potentiels.

concluded that the small increases in risk associated with antipsychotics should be balanced against medical need as well as efficacy and safety of alternatives.[66] The authors also suggested that consideration be given to early withdrawal of medications[66]; this is in keeping with evidence that for some patients antipsychotics might be safely discontinued without re-emergence of problem behaviours.[67]

In my opinion, these developments further underscore the need to begin with nonpharmacologic interventions for BPSD and to exercise caution when using drugs. The recommendation to consider atypical antipsychotics as first-line agents is under appropriate scrutiny. Antipsychotics should not be regarded as innocuous (or long-term) medications, and doctors—along with other decision makers—should weigh their risks against any potential benefits.

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Competing interests

I served on an advisory board for galantamine for Janssen-Ortho Inc.

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