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Pharmacological Treatment of Challenging Neuropsychiatric Symptoms of Dementia

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ABSTRACT

Neuropsychiatric symptoms of dementia can be challenging to patient and carers, and affect the majority of people with dementia at some stage. Symptoms including agitation, aggression, and psychosis may respond to non-pharmacological therapy. If pharmacotherapy is required the family and carers should be informed and involved in defining treatment goals and monitoring progress. The best current evidence is for atypical antipsychotics with two randomised controlled trials supporting the use of risperidone. However, there are concerns about an increased risk of stroke and death from atypical antipsychotics. Other drug classes have less supportive evidence for efficacy, but may be appropriate for specific symptoms. In all cases, attempts should be made to minimise the dose of the drug and cease it entirely after a time.

J Pharm Pract Res 2005; 35: 228-34.

INTRODUCTION

In Australia there are currently 200 000 people with dementia and this is projected to increase to 700 000 by 2050.¹ There are over 200 causes of dementia but the most prevalent are Alzheimer's disease (AD), vascular dementia, Lewy body dementia, frontotemporal dementia and mixes of these four. Cognitive deficits are the main features of dementia but non-cognitive symptoms are frequent. Functional impairment is required to diagnose dementia, and neuropsychiatric symptoms affect up to 90% of patients with dementia at some stage in their illness.²⁻⁷ These symptoms are often challenging and include psychosis, delusions, agitation, aggression, repetitive vocalisations, resistive behaviour and wandering. They may be the dominant presenting feature of the dementia, and a feature of the mild cognitive impairment that often precedes dementia.^{6,8}

Neuropsychiatric symptoms are associated with a range of adverse effects and outcomes. They can be distressing and burdensome, increase the likelihood of a move to a nursing home, and contribute to the cost of caring for someone with dementia.⁹⁻¹⁸ In residential care facilities, neuropsychiatric symptoms are frequent, with one study showing 34% of residents exhibiting such behaviour at least weekly.¹⁹ Overall prevalence ranges from 29 to 92% in Australian residential care facilities.^{20,21}

Neuropsychiatric symptoms can persist, as shown in a study of 329 people with dementia where 81% with neuropsychiatric symptoms at baseline had at least one symptom at an 18-month follow-up.²² Specific symptoms

may vary in persistence. In a study of patients with mild AD, activity disturbance (e.g. wandering) was persistent over two years but paranoia and delusional ideation were only moderately persistent, and depressive symptoms infrequently lasted more than a year.²³

While the cause of a particular neuropsychiatric symptom is usually difficult to determine, a number of mechanisms and associations have been found. Neurotransmitter abnormalities have been associated with these symptoms and this may provide a rationale for some of the pharmacological options.²⁴ Studies vary in their findings on the association of pre-morbid personality traits with neuropsychiatric symptoms.^{25,26} Psychosis in patients with AD aggregates within families, suggesting a genetic influence.²⁷ Similarly, apolipoprotein E status can predict delusions in AD.²⁸ The environment may also contribute to these symptoms, but this relationship is complex.²⁹ The correlates of aggressive behaviour have been recently reviewed and include the degree of cognitive impairment, personality, sensory change, physical illness, language impairment, affective and psychotic disorders.³⁰

It is desirable to manage challenging neuropsychiatric symptoms without medication and a first-line non-pharmacological approach is often successful.³¹⁻³⁴ Specific symptoms, such as apathy and refusing to eat, may respond better to a non-pharmacological approach.^{35,36} A range of non-pharmacological interventions have been evaluated in clinical trials with more recent evidence and reviews supporting music therapy, exercise and light therapy.³⁷⁻⁴⁰ However, it is inappropriate to persist solely with non-pharmacological approaches if the symptoms persist, are burdensome, and are of a type that may respond to pharmacotherapy.

PHARMACOLOGICAL TREATMENT

Prescribers should be aware of the major issues around drug use in older people. Older people consume more medicines—an average of 2.2 drugs per elderly community resident. Between 20 and 40% of older people in the community are taking five or more medicines.^{41,42} The number used in nursing homes is higher—an average of 6.75 drugs which is significant as the high prevalence of challenging neuropsychiatric symptoms in this group is more likely to lead to consideration of pharmacotherapy.⁴³ This high rate of drug use is one factor contributing to the high frequency of adverse drug events and this appears to have increased over the last 20 years.⁴⁴ In nursing homes, as many as 23% of all adverse drug events have been associated with neuroleptic drug use.⁴⁵ Prescribers should thus aim to reduce drug use in older people.^{46,47} In doing so they should avoid under-use of useful drugs; this may be a particular risk in residential care facilities.⁴⁸ The propensity for some antipsychotics to have anticholinergic effects

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is of particular relevance to the risk of adverse events.⁴⁹ This is of added concern as in a recent study 35% of people prescribed a cholinesterase inhibitor for dementia were also taking a drug with anticholinergic effects.⁵⁰ Other drugs used for challenging neuropsychiatric symptoms increase the risk of hypotension, some affect liver enzymes, and some are prone to drug interactions.

People handle drugs differently as they age and prescribers need to be aware of these altered pharmacokinetics and pharmacodynamics.^{51,52} In general, lower starting and target doses are recommended in older people.

A Finnish study found 87% of patients in nursing homes and acute geriatric wards were on at least one psychotropic drug, although not all prescriptions were necessarily for challenging behaviours.⁵³ A US study in residential care/assisted living found a prevalence of the use of psychotropic drugs of a little over 50%.¹⁹ A Canadian study of older adults admitted to a nursing home and who had no previous neuroleptic exposure found 17% were prescribed such a drug within the first 100 days.⁵⁴

Atypical Antipsychotics

Atypical antipsychotics have become a preferred treatment for psychosis, aggression and agitation in dementia, and the recent listing of risperidone for this indication on the Australian Pharmaceutical Benefits Scheme has increased its affordability. Risperidone is the most studied antipsychotic with three large randomised placebo-controlled trials in nursing home settings.⁵⁵⁻⁵⁷ In these trials patients were selected for baseline challenging neuropsychiatric symptoms and had AD, vascular dementia or a mixture of these. The primary endpoints included the Behavioral Pathology in Alzheimer Disease Rating Scale (BEHAVE-AD) and the Cohen-Mansfield Agitation Inventory (CMAI). Two of these trials were positive in their primary endpoints, demonstrating significantly reduced psychosis, agitation, aggression and related symptoms in individual trials (mean dose of risperidone was 1 mg daily). Two analyses of the pooled results showed statistically significant benefits across a range of neuropsychiatric symptoms (hitting, verbal aggression, restlessness, agitation, aimless wandering, non-paranoid delusions) but the most validated and successfully treated symptoms were psychosis, aggression and agitation.^{58,59} An analysis of the Australia and New Zealand trial also showed a statistically significant benefit on nursing burden associated with caring for the residents.⁶⁰

Other studies supporting the use of risperidone include a naturalistic study in Austria which is notable for the large number of patients (938) included.⁶¹ The overall efficacy of risperidone in treating neuropsychiatric symptoms was judged as 'excellent' by the general practitioners and carers in about half the patients and judged 'not satisfactory' in about 4% of cases. A double-blind randomised study of risperidone and haloperidol in 120 Korean patients with dementia also showed statistically significantly improved symptoms compared to baseline.⁶²

A review of trials of atypical antipsychotics for neuropsychiatric symptoms concluded that risperidone and olanzapine have the best evidence for efficacy.⁶³ There were three olanzapine studies including one negative study on psychosis in nursing home residents with dementia and a 24-hour intramuscular olanzapine study for acute disturbances.⁶⁴⁻⁶⁶ The positive long-term

study was conducted in nursing homes and showed that the two lower doses (5 and 10 mg/day) tested were effective as measured by three core symptoms in the NeuroPsychiatric Inventory Nursing Home scale (NPI-NH).⁶⁴

While the main rationale for the use of atypical antipsychotics has been their more favourable adverse effect profile than that of the older typical antipsychotics, there is increasing evidence that the atypical antipsychotics may also be more effective. In the Korean study, where patients were crossed over from risperidone to haloperidol in a double-blind fashion, significantly greater improvements on the BEHAVE-AD were seen with risperidone than with haloperidol.⁶² A recent meta-analysis of the efficacy of atypical antipsychotics in schizophrenia found greater effect sizes than for the older typical antipsychotics. The effect size differences were 0.25 ($p < 0.001$) for risperidone and 0.21 ($p < 0.001$) for olanzapine.⁶⁷ Some individual studies however have not shown a significant difference between haloperidol and risperidone.⁵⁷

Other atypical antipsychotics have been trialled for challenging neuropsychiatric symptoms of dementia but to date results have only been published for one of these drugs. In a randomised double-blind controlled trial in 93 residents of care facilities who had AD or other dementia and significant baseline agitation, quetiapine was not associated with any benefit over placebo on agitation at 6 or 26 weeks.⁶⁸ Aripiprazole has also been trialled for psychosis in AD with unpublished presentations noting equal improvements in active versus placebo treated groups. Posters have also described the frequency of use, but not efficacy, of ziprasidone in nursing home settings. Clozapine has also been used for challenging neuropsychiatric symptoms in dementia, and in psychosis complicating Parkinson's disease, which may be due to dementia or long-term dopaminergic therapy, or both.⁶⁹ It is favoured as it has been associated with a very low risk of extrapyramidal effects, but it is the most anticholinergic of the atypical antipsychotics so is best avoided in those who are already confused.⁷⁰ Quetiapine may also be associated with a lower risk of extrapyramidal effects and can be effective for psychotic symptoms in Parkinson's disease.⁷¹

Published expert opinion supports the use of atypical antipsychotics for challenging neuropsychiatric symptoms of dementia. In a survey of 52 American geriatric psychiatrists and geriatricians, the recommended therapy for agitated dementia with delusions was an antipsychotic alone, with risperidone first-line and quetiapine or olanzapine as second-line.⁷²

The adverse effects of atypical antipsychotics differ between agents and differ substantially from the older typical antipsychotics. Their major benefit over older antipsychotics is the lower risk of extrapyramidal adverse effects, although the newer antipsychotics are not completely devoid of such risks. Jeste et al. found the annual cumulative incidence of persistent tardive dyskinesia with risperidone was 2.6% but in another study by the same author the risk of tardive dyskinesia from risperidone was 5 to 6 times lower than that from haloperidol ($p < 0.05$).^{73,74} Lower doses of the newer antipsychotics further reduce this small risk. These antipsychotics should be used with great caution in those with Lewy body dementia because of the risk of worsening parkinsonism. As with psychosis in

Parkinson's disease, quetiapine has been successfully used in Lewy body dementia.⁷⁴ Parkinson's disease with dementia and Lewy body dementia may be part of a single disease spectrum. There are also isolated case reports of the other atypical antipsychotics being successfully used in Lewy body dementia.^{76,77}

The adverse effects arousing most concern are stroke and mortality. The Australian and New Zealand nursing home study was the first to find an unexplained increased risk of cerebrovascular events in those on risperidone compared to placebo and this increased risk has since also been found with olanzapine.^{55,78} When trials of risperidone and olanzapine in dementia were pooled, 2.2% of drug-treated patients experienced a cerebrovascular adverse event compared with 0.8% of placebo-treated patients.^{79,80} Many national regulatory bodies have issued warnings about this increased risk. A recent review concluded that most of these cerebrovascular events were non-serious and that large observational studies showed no such increased risk.⁸¹ This review also found that strokes were no more common with risperidone or olanzapine than with quetiapine, older antipsychotics or benzodiazepines. No mechanism behind these adverse events has yet been defined.

An increase in mortality in older people taking atypical antipsychotics has also been detected. In 17 placebo-controlled trials using risperidone, olanzapine, quetiapine or aripiprazole the mortality was 1.6 to 1.7 times that of placebo in the pooled active treatment arms.⁸² Most of these trials are unpublished and data were obtained from manufacturers. No clear mechanism has yet been isolated to explain this finding. National regulatory agencies and pharmaceutical companies have begun issuing warnings.

Other adverse effects include weight gain and diabetes, although these have not yet been found for risperidone.⁸³ Falls have also been reported but in ambulatory nursing home patients—risperidone 1 mg/day was associated with a 70% lower rate of falls compared to placebo although at 2 mg/day the rate exceeded that of placebo.⁸⁴ This again emphasises the desirability of using the lowest effective dose in older people. While clozapine is the most anticholinergic, olanzapine also has anticholinergic effects, which may further worsen cognitive performance. In a comparative trial, these effects were not found with risperidone.⁸⁵ The quetiapine study for agitation in care facility residents with dementia, did show a significant cognitive decline, compared to placebo, in the quetiapine-treated group, as measured by the Severe Impairment Battery.⁶⁸ One possible mechanism for this could be the anticholinergic effects of quetiapine, which are twice as great as those of risperidone but less than those of olanzapine and clozapine.⁶⁸ In a population study, long-term psychotropic drug use (including antipsychotics) was not found detrimental to cognitive function.⁸⁶ Rarer adverse effects of these drugs include hyperprolactinaemia, osteoporosis and agranulocytosis, but these have largely been reported from studies in younger people or from studies where higher doses were used.^{87,88} Theoretically, the combination of falls and osteoporosis, along with anticholinergic effects, could increase the risk of fractures, but this has not been shown in controlled trials.

Cholinesterase Inhibitors

Cholinergic deficits may underlie some of the neuropsychiatric features of dementia, providing a rationale for the use of cholinergic therapies including cholinesterase inhibitors.^{24,89} Two meta-analyses and six randomised controlled trials of various cholinesterase inhibitors have been recently reviewed and further studies continue to be published.^{63,90} Five of the eight reviewed papers, including the two meta-analyses, showed statistically significant benefits on at least one primary neuropsychiatric endpoint, compared with placebo, but the magnitude of effect was generally small. These trials however did not select patients for baseline neuropsychiatric symptoms. The UK study of people with baseline agitation and dementia included a rivastigmine arm and a quetiapine arm, and failed to show any improvement from rivastigmine in agitation, compared to placebo.⁶⁸ Reduced carer distress has been associated with higher doses of galantamine.⁹⁰ In another study, antipsychotic use was lower in patients on rivastigmine for AD.⁹¹ The overall use of antipsychotics was 9.8% in the 497 patients on rivastigmine compared to 26% in the 749 on no cholinesterase inhibitor.

The adverse effects of cholinesterase inhibitors include nausea, vomiting, diarrhoea, weight loss, bradycardia and a risk of exacerbating asthma or peptic ulceration. These effects are less common at lower doses and reduced if dose increases are no more frequent than every four weeks.

Memantine

Two trials that used memantine (N-methyl-D-aspartate receptor antagonist) either as monotherapy or in addition to donepezil reported NeuroPsychiatric Inventory (NPI) scores as secondary outcomes.^{92,93} Patients were not selected for neuropsychiatric symptoms. One trial showed patients receiving memantine improved on the NPI by an average of 0.1 points compared to a 3.7 point decline in the placebo group ($p = 0.002$).⁹² This small difference, in a 120-point scale, may be clinically insignificant. In the other trial, the NPI scores did not significantly differ between the two groups.⁹³ There have also been trials of memantine for vascular dementia and an unpublished trial in mild AD.⁹⁴ A recent Cochrane review concluded memantine did have favourable effects on behaviour in mild to severe AD and in vascular dementia.⁹⁵ Adverse effects are uncommon, and include dizziness and agitation.

Mood Stabilisers

There have been three randomised controlled trials of valproate for neuropsychiatric symptoms.⁹⁶⁻⁹⁸ None showed significant differences between placebo and valproate-treated groups across primary outcomes. The two small randomised controlled trials with carbamazepine, which included a total of 72 patients, showed a statistically significant improvement in agitation in one trial, but no improvement in the primary outcome in the other trial.^{99,100} The current evidence is insufficient to support the use of either of these drugs. Open-label and extension trials have also been completed, but provide less robust evidence.¹⁰¹ These drugs have a range of adverse effects including haematological toxicity and drug interactions. There has been a recent black-box warning in the USA regarding carbamazepine.

There have been no randomised placebo-controlled trials of lithium or gabapentin for neuropsychiatric symptoms. An open-label trial of gabapentin in 20 patients has suggested efficacy but this remains to be established by more rigorous trial design.¹⁰²

Antidepressants

Only one of five randomised controlled trials of selective serotonin reuptake inhibitors showed benefit in neuropsychiatric symptoms. This trial in 52 hospitalised patients found a significant 10-point change (of 168 points) in the Neurobehavioural Rating Scale in those randomised to citalopram 20 mg daily, compared with a 2.3 point change for placebo ($p < 0.001$).¹⁰³ The other four trials, involving fluoxetine, trazodone and sertraline, were negative on neuropsychiatric endpoints although a subgroup analysis of responders in one sertraline trial showed less depression.¹⁰⁴⁻¹⁰⁷ There has recently been a trial of trazodone in frontotemporal dementia which was negative for the primary endpoints.¹⁰⁸ On current evidence, selective serotonin reuptake inhibitors may be appropriate for depression in dementia but not for other neuropsychiatric symptoms. They are generally well tolerated although well recognised adverse effects include nausea, hyponatraemia and insomnia.

Benzodiazepines

While benzodiazepines are frequently used to reduce agitation and promote sleep in older people with dementia, there has only been one randomised controlled trial for neuropsychiatric symptoms.⁶⁵ This 24-hour trial of intramuscular lorazepam versus placebo (there was also an olanzapine arm) showed a significant benefit on the Positive and Negative Syndrome Scale-Excited Component, a measure including agitation. Other double-blind trials have not included a placebo arm. One compared oxazepam with haloperidol and diphenhydramine and two studies from the 1970s compared diazepam and thioridazine.¹⁰⁹⁻¹¹¹ All three of these trials suggested some efficacy for the benzodiazepines. As benzodiazepines have a range of adverse effects in older people, such as falls and fractures, their use for neuropsychiatric symptoms cannot be recommended on the weight of current evidence, apart from short-term use for agitation.¹¹²⁻¹¹⁴

Other Drugs

Reduced levels of oestrogen and excess testosterone have been associated with aggressive behaviours so manipulation of these hormones may assist in the control of aggression in dementia. Oestrogen has been used in a trial of 14 women and two men with moderate to severe dementia and aggressive behaviour.¹¹⁵ Oestrogen was associated with lower total aggression scores ($p < 0.03$) and decreased frequency of physical aggression ($p < 0.019$). An open-label trial of the anti-androgen cyproterone acetate in two demented male patients successfully reduced problematic sexual activity.¹¹⁶ Larger trials are needed before hormone therapy can be recommended for neuropsychiatric symptoms.

Older people with dementia report pain poorly, resulting in under treatment of pain, and pain may lead to agitation and other neuropsychiatric symptoms.¹¹⁷⁻¹¹⁹ In a single-blind crossover trial of a long-acting opioid in severely demented nursing home residents with agitation despite psychotropic therapy, there was no

significant improvement in the CMAI.¹²⁰ A subgroup analysis of the 13 patients above 85 years did show a benefit (mean change in CMAI score 6.4, 95% CI: 10.96-1.8). An earlier trial of morphine has not been reported in a peer-review publication but suggested a benefit.¹²¹ It is unclear whether benefit was from analgesia or other effects of opioids. While it is important to identify and treat pain in older people with dementia, the use of opioids for neuropsychiatric symptoms cannot currently be recommended, especially as they have a range of adverse effects including constipation.

There have been no randomised controlled trials of buspirone, an anxiolytic, although older case reports and an open-label study have suggested benefits.¹²²⁻¹²⁴

Beta-blockers have been trialled for a range of disruptive behaviours. In one randomised placebo-controlled trial, 31 nursing home residents with AD and neuropsychiatric symptoms that interfered with necessary care were included.¹²⁵ A mean dose of propranolol of 106 mg daily was significantly more effective than placebo in improving overall behavioural status as measured by the total NPI score and the Clinical Global Impression of Change. On individual NPI items, propranolol significantly benefited agitation/aggression, compared to placebo. In frail elderly people there are a range of contraindications to beta-blockers, including more severe peripheral vascular disease and bradycardia, and careful monitoring for adverse effects is vital.

PRACTICAL ISSUES

Assessment of Patient

In fully assessing the patient, particular attention should be paid to the issues in Table 1. A history should be taken from carers/family, and, where possible, the patient. A full physical examination is needed, and appropriate investigations requested.

Table 1. Issues to consider in patient assessment

- | |
|--|
| 1. Does the patient have dementia?
-exclude other psychiatric illness |
| 2. Is delirium present?
-even with coexisting dementia
-if so, assess for cause (usually reversible) |
| 3. Is the patient in pain?
-if so, treat |
| 4. Are other conditions contributing (even without delirium)
-consider and treat where possible infections, metabolic disturbances, adverse effects of medications, sensory impairments |
| 5. What are the features of the neuropsychiatric symptoms?
-onset, precipitants, time of day, duration, frequency |
| 6. Does the neuropsychiatric symptom require treatment?
-is it disturbing others, or the patient? |
| 7. Have appropriate non-pharmacological approaches been trialled?
-if not, they should be trialled first unless behaviour is very severe/acute |
| 8. Is it a neuropsychiatric symptom that has been shown to respond to medication?
-agitation, psychosis, aggression, delusions and depression have best evidence
-little evidence for wandering, resistiveness, apathy |
| 9. Consider other medications
-may be precipitating the behaviour
-may be possible to cease, even if not causing a current adverse event
-may interact with planned therapy |

Defined Target Symptoms and Measures of Success

The treatment team should clearly define the specific symptoms that are being treated. It is not sufficient to aim for the patient to be 'more manageable' or to seem more content. Once specific symptoms have been defined, criteria for success of therapy should be ascertained. This may include psychotic episodes reduced from daily to weekly (or better), or no further aggression.

Obtain Consent and Inform

The patient's family should be informed of the proposed pharmacotherapy, including risks, and give consent to therapy. This is especially important with current data about the increased risk of stroke and mortality associated with atypical antipsychotics. This should, however, be put into context. Risperidone, for instance, has proven efficacy and the increased risk of adverse events may be considered by the family to be outweighed by the suffering caused by persistent psychosis, delusions, aggression or agitation. As there are no more effective drugs and it appears others are also associated with an increased risk of serious adverse events, the family may agree to a trial of therapy.^{73,81} It is inappropriate to not offer this therapy based on current data. Where possible, the patient should also participate in this process, but even assent may be difficult to obtain from more severely demented people.

Select the Appropriate Drug

The best evidence exists for atypical antipsychotics but other drugs may be considered for specific symptoms (Table 2). Thus, a selective serotonin reuptake inhibitor is more appropriate for depression, and a benzodiazepine may be an acceptable choice for acute agitation (as well as searching for a cause of this acute change). Other drugs may need to be considered if the risk of adverse effects, or their occurrence, leads to an atypical antipsychotic not being chosen. The recent trial with quetiapine showing no benefit for agitation and a decline in cognition should at this stage lead to considerable caution in its use for neuropsychiatric symptoms in dementia.⁶⁸ The strength of evidence for the various drugs has been reviewed extensively above, but lack of conclusive evidence from trials does not mean a particular drug will be ineffective. The prescriber should be aware of a strong placebo effect seen in most trials in this area, although that itself is an acceptable way of achieving targets.

Table 2. Drugs for neuropsychiatric symptoms of dementia

Drug	Starting dose	Maximum dose
Citalopram	10 mg daily	20 mg daily
Donepezil	5 mg daily	10 mg daily
Galantamine	8 mg daily	24 mg daily
Memantine	5 mg twice daily	10 mg twice daily
Olanzapine	2.5 mg daily	10 mg daily
Oxazepam	7.5 mg twice daily	30 mg twice daily
Quetiapine	12.5 mg twice daily	50 mg twice daily
Risperidone	0.25 mg twice daily	1 mg twice daily
Rivastigmine	1.5 mg twice daily	6 mg twice daily
Sertraline	25 mg daily	100 mg daily
Valproate	200 mg twice daily	1000 mg twice daily

Monitor Patient

Patients should be regularly monitored for achievement of treatment goals and adverse effects. Concordance should also be assessed. The scales used in trials are usually not practical in clinical settings, but should be considered if a more objective assessment is needed. The most useful scales in this respect are the CMAI, NPI (NPI-NH if in nursing home care) and BEHAVE-AD.

Withdraw Therapy

Although some neuropsychiatric symptoms may be persistent, they may not persist in an individual.²² Always consider withdrawing therapy once symptoms have improved—such withdrawal can be considered within three months although a shorter time frame may be appropriate for more acute symptoms. It is best to gradually reduce the dose (over several weeks) monitoring for recurrence or worsening of target symptoms. If symptoms do recur or deteriorate, the dose should not be further lowered and may need to be increased again if warranted. A further attempt at withdrawal can be made later. Even achieving a lower dose is a success if symptom control remains adequate. In the presence of adverse effects it is desirable to cease the drug, but minor adverse effects (e.g. mild sedation) may be an acceptable price to pay for symptom control. Several small trials have assessed withdrawal of antipsychotics in patients with dementia. In one, there was no significant difference in withdrawal in those randomised to ongoing antipsychotics or placebo.¹²⁶ In another trial the withdrawal group showed reduced sleep efficacy compared to the ongoing therapy group.¹²⁷

CONCLUSION

Neuropsychiatric symptoms of dementia can be very distressing. The current issues around serious adverse effects from atypical antipsychotics have left prescribers with few if any equally effective and safer alternatives for aggression, agitation, psychosis and delusions. In each case, where pharmacotherapy is warranted, a considered decision should be made by the family and, if possible, the patient. Other drugs may be preferred to an antipsychotic if the family feel the risks of the proposed atypical antipsychotic is too high. At all times, patients should be carefully monitored with a view to ceasing or reducing the dose at an appropriate time. Ultimately, prevention or delay of dementia will reduce the burden of these symptoms in society, but prevention is not generally possible.¹²⁸

Competing interests: The author has conducted research and/or served on advisory boards for Bristol Myer Squibb, Merck Sharp & Dohme, Servier, Sanofi Synthelabo, Pfizer, Amgen, AstraZeneca, Janssen-Cilag, Novartis, Lundbeck, Roche and Eli Lilly.

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Submitted: April 2005

Accepted after external peer review: August 2005