

Role of antipsychotics in managing behavioural and psychological symptoms of dementia

Key Messages

- Manage underlying causes of behavioural and psychological symptoms of dementia and try behavioural interventions.
 - Use an antipsychotic only if aggression, agitation or psychotic symptoms cause severe distress or an immediate risk of harm.
 - There is no conclusive evidence that any antipsychotic is more efficacious than another. Risperidone causes less tardive dyskinesia than haloperidol and is PBS listed for managing behavioural symptoms.
 - Monitor closely when starting therapy to ensure the target behaviour improves and that adverse effects are tolerated.
 - Review the need for continuing antipsychotic therapy within 3 months and regularly afterwards. Withdrawing antipsychotic treatment may not worsen behaviour.
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'Behavioural and psychological symptoms of dementia' (BPSD) refers to the often distressing non-cognitive symptoms of dementia, including agitation and aggressive behaviour. Other common terms for these symptoms include neuropsychiatric symptoms of dementia, non-cognitive symptoms of dementia, challenging behaviours of dementia, or behavioural disturbances in dementia.¹

Assess underlying causes and contributing factors

Consider underlying causes and contributing factors of problem behaviours

When a person with dementia exhibits behaviours of concern:

- review possible physical causes of distress or delirium (e.g. pain, infection, dehydration, hyponatraemia, constipation, hearing or vision problems)
- examine the medication regimen (especially for anticholinergic drugs, which can impair cognition)
- look for contributing environmental factors (e.g. noise, poor lighting, conflict with carers)
- consider other psychiatric diagnoses (e.g. depression, anxiety).^{2,3}

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National Prescribing Service Limited

ABN 61 082 034 393 | Level 7/418A Elizabeth Street Surry Hills NSW 2010 | PO Box 1147 Strawberry Hills NSW 2012
Phone: 02 8217 8700 | Fax: 02 9211 7578 | email: info@nps.org.au | web: www.nps.org.au

Non-drug strategies

Tailor management to the individual, combining non-drug strategies as appropriate

Support services (listed in Box 1) can provide advice on simple behavioural interventions. Information is included in the RACGP's *Medical care of older persons in residential aged care facilities* (the 'silver book', available online) and in Alzheimer Australia's publication *Reducing behaviours of concern*.^{4,5} Some examples of interventions are:

- music
- pet therapy
- exercise
- carer training
- reminders and repetition of information
- regular social activity, groups and visitors.⁴

Choose a combination of strategies according to the patient's needs and available care and resources. Individually tailored interventions appear to be particularly effective.⁶ Interdisciplinary collaborative care offering a variety of interventions according to need resulted in significant improvement in BPSD in one randomised controlled trial involving community-dwelling people with moderate dementia. Behavioural interventions included carer education and advice about lighting and music. The collaborative care protocols also resulted in more prescribing of cholinesterase inhibitors and antidepressants.⁷

Encourage carers and people with dementia to seek support

Interventions directed at carers, such as counselling, support groups, education and training, may help to reduce carer distress and improve the patient's mood.

Information and support services for carers and people with dementia are listed in Box 1 on the back page of this document.

Antipsychotics are second line

Use drug therapy only if behaviours cause severe distress or an immediate risk of harm

The adverse effects of antipsychotic drugs in people with dementia are considerable and should be balanced against the modest efficacy of treatment. Antipsychotic drugs should only be prescribed after an individual assessment of the benefits and harms⁸, and as an adjunct to non-drug strategies. Discuss treatment choices with carers or family members when possible.

Aggression, agitation and psychotic symptoms (e.g. delusions or hallucinations) respond best to antipsychotic therapy. Many troublesome symptoms are unlikely to respond. These include:

- wandering
- withdrawal
- cognitive defects
- touching
- shouting
- insomnia
- pacing
- incontinence.^{3,9,10}

Risperidone is the preferred antipsychotic for use in BPSD

Therapeutic Guidelines: Psychotropic recommends, in order of preference¹¹:

Atypical antipsychotics		
Risperidone Risperdal	0.5–2 mg orally, daily in 1 or 2 doses	PBS authority
Olanzapine Zyprexa	2.5–10 mg orally, daily in 1 or 2 doses	not PBS listed*
Conventional antipsychotics		
Haloperidol Serenace	0.5 mg orally (at night) to 2 mg twice daily	PBS unrestricted

* Olanzapine does not have a TGA-approved indication for BPSD. Prescribing for BPSD is private prescription only and off label

Start with the minimum dose and increase by 100% every 3–4 days until the symptoms are controlled or the maximum dose is reached. Use the minimum effective dose, as adverse effects (e.g. extrapyramidal symptoms) are dose related. Aim for once-daily (e.g. afternoon or evening) dosing to minimise daytime motor slowing.

The efficacy of as-required (prn) dosing of antipsychotics in BPSD has not been evaluated in clinical trials. Prescriptions for prn dosing should only be used with a stated specific indication, and for at most 2 weeks before review.

Risperidone has the most evidence for efficacy in managing BPSD among all antipsychotics. Nevertheless, published comparisons provide no conclusive evidence that risperidone is more or less efficacious than haloperidol or olanzapine.^{12,13}

Risperidone and olanzapine are preferred over haloperidol because of their reduced tendency to produce movement disorders. While a few head-to-head trials have failed to demonstrate differences in adverse effects in the short term, observational data suggest that the incidence of irreversible tardive dyskinesia with haloperidol is substantially higher.¹⁴

Antipsychotics have at best a small positive effect on behaviour

Risperidone and olanzapine have a statistically significant but modest beneficial effect on aggression in patients diagnosed with Alzheimer’s disease.¹⁵ Data from placebo-controlled trials suggest that 5–14 people must be treated for 1 additional person to show clinically significant improvement in BPSD over 12 weeks.¹⁶ However, these estimates are probably inflated by selective reporting.¹⁶ There is insufficient evidence to evaluate the efficacy of aripiprazole (Abilify) or quetiapine (Seroquel).¹⁵

Efficacy is countered by high dropout and adverse-event rates, and appears to translate into poor clinical effectiveness. In the CATIE-AD phase 1 trial, patients discontinued active treatment with an antipsychotic at the same rate as placebo, after an average of about 8 weeks, mostly because of adverse effects or lack of efficacy.¹⁷

Placebo response rates in trials were 20% or higher, indicating that BPSD often resolves spontaneously within 12 weeks.^{16,17}

There is insufficient evidence to recommend drugs other than antipsychotics in BPSD

Benzodiazepines, anticonvulsants, beta blockers, cholinesterase inhibitors or antidepressants should not be used routinely to manage behavioural symptoms.¹⁸

Benzodiazepines have some evidence of efficacy and may be useful for short-term treatment of severe anxiety or agitation. However, they are associated with falls, somnolence and cognitive impairment and have the potential to worsen aggressive behaviour through disinhibition.^{11,19}

Avoid haloperidol in patients with Lewy body dementia, and use risperidone and olanzapine cautiously

Dementia with Lewy bodies accounts for up to 10% of dementias. It is diagnosed clinically as dementia with any two of complex visual hallucinations, fluctuating cognitive impairment or spontaneous motor parkinsonism.¹¹

Conventional antipsychotics (e.g. haloperidol) cause dangerous extrapyramidal symptoms in people with Lewy body dementia, with risk of neuroleptic malignant syndrome.^{20,21}

While atypical antipsychotics (e.g. risperidone and olanzapine) may be used with caution, adverse effects are common.²⁰ Some guidelines recommend cholinesterase inhibitors (donepezil [Aricept] or galantamine [Reminyl]) for managing BPSD in Lewy body dementia, although evidence of efficacy is limited.⁸

Prepare a treatment plan and monitor closely when starting therapy

Monitor for efficacy, adverse effects and general health

When initiating antipsychotic therapy:

- assess the target behaviour daily
- measure blood pressure at baseline and within the first 7 days of treatment
- check body weight, lipids and fasting plasma glucose at baseline
- observe closely for signs of extrapyramidal symptoms (e.g. abnormal movements of the face, arms, legs or trunk) or anticholinergic effects (e.g. dry mouth, constipation, urinary hesitancy or delirium).^{9,11}

Discontinue treatment if there is no improvement in the target behaviour

Response usually occurs in 1–2 weeks and clinical improvement should be expected within 12 weeks.^{16,22}

Discontinue if there is no improvement, and reassess. Avoid stopping abruptly — taper the dose by 50% every 2 weeks and stop after 2 weeks on the minimum dose. Other non-pharmacological approaches or an alternative antipsychotic may be tried.

People with dementia are at risk of serious adverse effects

Several antipsychotics increased the risk of death in clinical trials, and others may do so as well

An increased death rate was found in an analysis of placebo-controlled trials of aripiprazole, olanzapine, quetiapine and risperidone in dementia patients, mostly due to cardiovascular events (e.g. heart failure, sudden death) or infections (e.g. pneumonia).²³ One death was associated with antipsychotic use for every 100 patients treated over 10–12 weeks.²⁴

Both olanzapine and risperidone were associated with an increased risk of fatal and non-fatal strokes and transient ischaemic attacks.^{21,25} Other antipsychotics (including older drugs such as haloperidol) may carry similar risks of death or stroke, but there is insufficient evidence to draw conclusions.^{23,24}

Use antipsychotics with caution when patients have known cardiovascular disease (e.g. heart failure, cerebrovascular disease or history of myocardial infarction).^{11,21}

Adverse effects are common with antipsychotics but their nature may vary from drug to drug

In a head-to-head trial, significantly more patients assigned to olanzapine discontinued within 12 weeks because of adverse events, compared with patients assigned to risperidone (16% vs 9%). Risperidone (average dose 1 mg/day) caused significantly worse extrapyramidal symptoms than olanzapine (average dose 5 mg/day). Somnolence, abnormal gait, urinary incontinence and hostility were common with both drugs, but not placebo.¹³

In the CATIE-AD phase 1 trial, both olanzapine and risperidone caused significantly more extrapyramidal symptoms, sedation, weight gain and confusion than placebo. About 5% of those taking olanzapine or risperidone discontinued because of extrapyramidal symptoms. Only patients taking risperidone experienced elevated serum prolactin concentrations.¹⁷

The long-term risk of diabetes is unclear

There are few data regarding the incidence of diabetes in people with dementia who are using antipsychotics. Epidemiological studies have found an association between the onset of type 2 diabetes and using clozapine (Clopine, CloSyn, Clozaril) or olanzapine, or, in some studies, risperidone or quetiapine, but these studies included few elderly people with dementia.²⁶

Regularly review the need for continuing therapy

Review at least every 3 months

Review the target behaviour, changes in function and treatment-related adverse effects every 3 months or according to clinical need.⁸ If symptoms are stable, try gradual dose reductions and potentially withdrawal every 6 months, as BPSD is often temporary.¹¹

Several studies have reported that most patients taken off antipsychotic treatment for BPSD showed no worsening of behaviour.^{27,28}

Box 1: Information and support services for carers and people with dementia

Alzheimer's Australia (see www.alzheimers.org.au) and State-based Alzheimer's associations

- Co-ordinate support groups, information sessions and free specialist counselling services for carers and patients.
- Provide help sheets on aspects of caring for people with dementia.

National Dementia Helpline (Ph 1800 100 500)

- Provides practical information, advice and support for people with dementia, their family and carers.
- Available 24 hours a day.
- Provided by Alzheimer's Australia.

Aged and Community Care Information Line (Ph 1800 500 853)

Provides information about:

- Community Aged Care Packages.
- Residential care fees in Australian Government-funded facilities.
- Aged Care Assessment Teams.

Commonwealth Carer Resource Centres (Ph 1800 242 636)

- Provide information about services and support for carers.
- Co-ordinate the National Carer Counselling Program, which provides short-term counselling to reduce carer stress, improve carer coping skills and facilitate continuation of the caring role.

Expert reviewer

Dr. David Kitching
Specialist in Psychiatry of Old Age
Chair, Committee on Psychotropic Drugs
and other Physical Treatments,
RANZCP

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- Online citations available at www.nps.org.au/healthpro

The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decisions based on this information should be made in the context of the clinical circumstances of each patient.



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