

Antipsychotics in people with dementia – an update and reminder

Key concepts:

- Non-pharmacological treatments for the behavioural and psychological symptoms of dementia (BPSD) should be trialled initially before considering drug therapy
- Antipsychotics have limited clinical effectiveness for most features of BPSD
- An antipsychotic is only indicated if aggression, agitation or psychotic symptoms cause severe distress or an immediate risk of harm to the patient or others
- Concurrent non-pharmacological measures should be employed along with drug treatment
- Start with the lowest possible dose, and if a dose increase is necessary, titrate slowly to effect
- Regularly review the patient for clinical response and adverse effects

The Antipsychotics in Dementia (A4D) programme was launched in October 2008 and included a special edition of Best Practice Journal, “Antipsychotics in Dementia”, a supporting website and a practice review activity. The focus of the programme was to provide education and guidance on the safe use of antipsychotics in the treatment of behavioural and psychological symptoms of dementia (BPSD) in aged care facilities.

The following is a reminder and update of the key points of the programme along with some results and comments from the practice review. What are the risks and benefits of antipsychotics for BPSD?

What are the risks and benefits of antipsychotics for BPSD?

It is well recognised that antipsychotics provide relatively few clinical benefits for people with dementia and in some cases pose a serious risk of an adverse outcome. Methodological problems make it difficult to provide precise figures for the benefits and risks.



Common manifestations of BPSD³

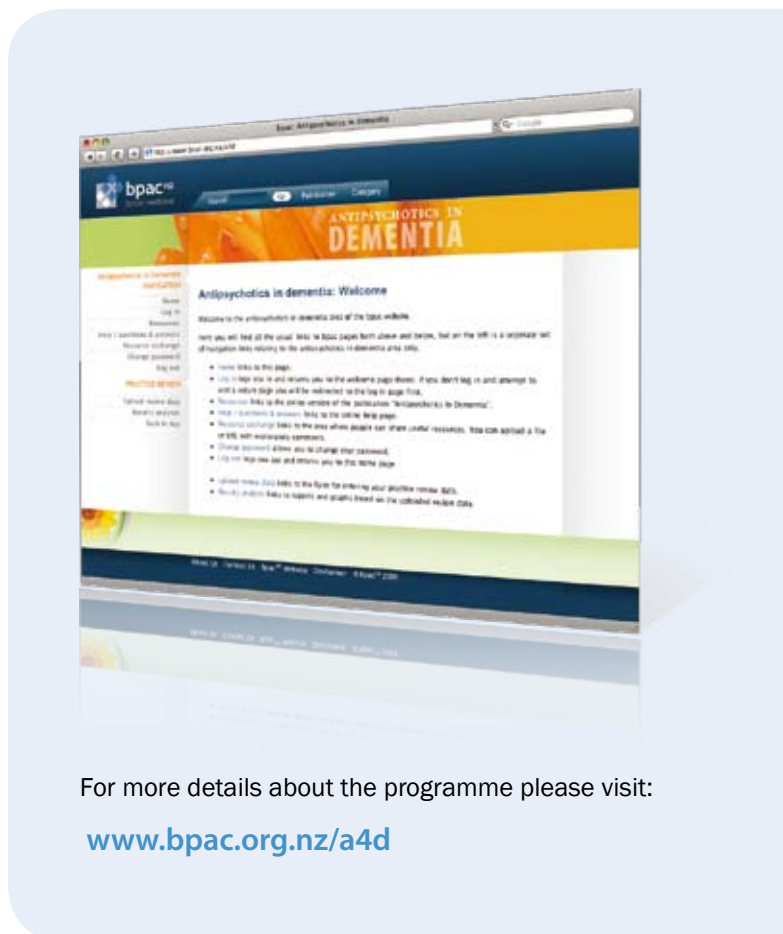
- Aggression
- Agitation or restlessness
- Anxiety
- Depression
- Psychosis, delusions, hallucinations
- Repetitive vocalisation, cursing
- Sleep disturbance
- Shadowing (following the carer closely)
- Wandering
- Non-specific behaviour disturbance e.g. hoarding

A recently commissioned review for the UK National Health Service predicts that for **every 100 people given an antipsychotic only 20 will derive some clinical benefit and there will be one extra death and one extra stroke.**¹ Antipsychotics should not be initiated without careful consideration and repeat prescribing should be limited to those who are obviously benefiting.

Non-pharmacological treatment of BPSD

Non-pharmacological treatment should be trialled initially, before considering drug therapy, as antipsychotics have limited clinical effectiveness for BPSD. Interventions should be tailored to the individual and the impact carefully monitored. A balance is necessary as excessive stimulation or over-activity may be counterproductive.

Most recommendations are based on best practice guidelines and institutional experience of what has been shown to work. A systematic literature review has provided evidence to support the effectiveness of activity programmes such as music, behaviour therapy and improvements to the physical environment.²



For more details about the programme please visit:

www.bpac.org.nz/a4d

Improvements in the environment can have a positive impact on symptoms of BPSD

People with dementia have memory and cognitive impairment, and problems in the design and configuration of residential facilities can cause or exacerbate restlessness, frustration, anxiety and disorientation. Some simple changes in the environment that can be beneficial include:³

- Moderating noise and other levels of stimulation
- Increasing signage and access to toilets
- Ensuring the surroundings are well lit
- Improving time orientation (e.g. prominent calendar and clock)
- Making the environment as “homelike” and reassuring as possible
- Separating non-cognitively impaired residents from people with dementia
- Small scale group living
- Any measure to reduce stress levels
- If possible, consistency of caregivers and other staff

Recreational activities may enhance quality of life and well being

Activities such as art, music, crafts, cooking, games and interaction with pets stimulate the person with dementia to become involved in a meaningful and enjoyable activity. Involvement in recreation may improve communication and self esteem.

Useful activities for the management of BPSD may include:

- Exercise
- Gardening
- Music
- Art
- Pet therapy
- Walking
- Group activities e.g. singing or craft
- Maintaining routine

Behaviour management may improve symptoms of depression

Behaviour management is defined as a structured intervention usually carried out by caregivers under expert supervision.³

Behaviour management involving pleasant events or problem solving has been shown to improve symptoms of depression in people with dementia.⁴

Pharmacological treatment of BPSD

Indications for antipsychotics

BPSD refers to a spectrum of quite diverse symptoms which cannot be placed under the same treatment umbrella. The important message is that antipsychotics are not effective for all BPSD.

There is some evidence that typical (e.g. haloperidol) and atypical (e.g. risperidone, quetiapine) antipsychotics are effective for psychotic symptoms (e.g. delusions or hallucinations) associated with dementia, or for people who are aggressive or agitated without psychoses. An antipsychotic is only indicated if the symptoms cause severe distress or an immediate risk of harm to the patient or others. Unless immediate drug treatment is required, standard non-pharmacological measures should be tried first. A trial of drug treatment should be viewed as a short term strategy and reviewed at least every three months.

At best, the effectiveness of antipsychotics for BPSD is modest. For example, data from placebo-controlled trials involving risperidone and olanzapine suggest that **5 to 14 people need to be treated for 12 weeks for one additional person to show significant improvement in aggressive symptoms associated with dementia.**⁵

Symptoms that do not usually respond to an antipsychotic include wandering, social withdrawal, shouting, pacing, touching, cognitive defects and incontinence.⁶ These symptoms may respond to interventions such as improvements to the environment.

It is important to realise that psychotic symptoms may be present without causing concern to the person or others, and in this setting close observation and non-pharmacological management are appropriate.

Drug selection


Haloperidol and risperidone have most commonly been used in BPSD. They do not differ significantly in clinical effectiveness for BPSD. At low doses, and in short term use, there are no appreciable differences in extrapyramidal effects, but haloperidol is associated with a greater risk of tardive dyskinesia.

Haloperidol is often suitable for the short term treatment of delirium or for aggression, agitation or psychoses. For longer term treatment an atypical agent such as risperidone is preferred. However, it should be recognised that risperidone behaves like a typical antipsychotic at higher doses, with the associated increased risk of extrapyramidal effects.

Olanzapine offers no clinical advantage over the other antipsychotics used for BPSD and has anticholinergic adverse effects. It is often associated with rapid and significant weight gain.

It appears that quetiapine is being increasingly used in older people. However there is little evidence to support its effectiveness in BPSD and it can cause significant postural hypotension and sedation.

Neither quetiapine or olanzapine have an indication in New Zealand for the treatment of symptoms associated with dementia.

 See page 30 for more information about quetiapine.

Start low and go slow

If a trial of antipsychotic treatment is considered necessary the starting dose should be as low as possible. This is particularly important for those people who are older, frail or at increased risk of falling. The starting dose can be divided or timed according to the behaviour, e.g. a lunchtime dose for those patients exhibiting increased agitation towards the end of the day (“sundowning”).

Dose increments should be modest and occur at no less than weekly intervals depending on response. Prior to starting a treatment trial, it is advisable to document what

Table 1: Recommended starting and maintenance doses for antipsychotics

Drug	Initial Daily Dose	Maximum Daily Maintenance Dose	Comments
Haloperidol	0.25 mg	Up to 2 mg twice daily	Initial dose of 0.5 mg can be given at night
Risperidone	0.25 – 0.5 mg	2 mg	1 or 2 divided doses
Olanzapine*	2.5 mg	10 mg	1 or 2 divided doses
Quetiapine*	12.5 mg	100 mg	Needs divided dosing

* Not approved in New Zealand for dementia related psychoses

will constitute a worthwhile clinical response, the duration of treatment and the maximum dose. Avoid high doses or prolonged use of antipsychotics that have not significantly improved the target behaviour. Recommended starting and maintenance doses are given in Table 1.

Maintenance

Initiation of treatment with an antipsychotic should be considered only as a trial to establish whether there is a reduction in the intensity and/or frequency of target behaviours. Carers must know what key adverse effects to monitor. Ongoing dose increases only tend to worsen adverse effects.

Maintenance treatment may be appropriate for those who have demonstrated a clear benefit from antipsychotic treatment without undue adverse effects, and where a trial dose reduction has resulted in reappearance of the target problem. A formal monitoring plan to assess changes in response and the significance of adverse effects should be in place. The prescriber should review the target behaviour, changes in function and significance of adverse effects at least every three months. ⁷

Monitoring

Routinely monitor for adverse effects such as constipation, sedation, postural hypotension and extrapyramidal effects. Additional monitoring may be appropriate, e.g. blood glucose and weight measurement with olanzapine.

Withdrawal

BPSD are often temporary, so if symptoms are stable, gradual dose reduction and eventual withdrawal can be tried. Studies have reported that most patients who are taken off an antipsychotic for treatment of BPSD showed no worsening of behavioural symptoms.^{8,9}

Withdrawal of antipsychotics should be done gradually, e.g. by reducing the dose by 50% every two weeks then stopping after two weeks on the minimum dose, with monitoring for recurrence of target behaviours or emergence of new ones. The longer a medication has been prescribed, the slower the withdrawal period needed.

Reasons for continuing antipsychotics include:

- An assessment of high risk of adverse consequences if they are withdrawn, especially if treatment has only been partially effective or prior relapses have occurred
- When the consequences of symptom relapse are deemed to be unacceptably severe
- When no alternative treatment approaches have been possible or effective in the past

Decisions to continue antipsychotics should be documented and include expected benefits and potential risks of ongoing treatment.

Results of practice review

After receiving A4D programme material, aged care facilities were invited to complete a review of their practice. A total of 312 patients were reviewed in 36 facilities. The most frequently prescribed antipsychotics for BPSD were risperidone (37%), quetiapine (28%) and haloperidol (13%).

This was a relatively small sample and the survey was not scientifically validated, but the collated responses to some of the questions suggest several areas where practices could be improved, especially in the documentation and review of antipsychotic use for BPSD.

- In 64% of patient notes there was no record that withdrawal of the antipsychotic had been attempted.

Comment: for most patients, withdrawal of the antipsychotic should be attempted and this should be documented in the patient record.

- Monitoring for adverse effects was only mentioned in the patient record in 35% of cases.

Comment: there should be a clear record of what adverse effects to look out for especially during initial dose titration.

- For about 30% of patients there was no clear record that target behaviours were identified before prescribing.

Comment: target behaviours should always be identified before prescribing an antipsychotic.

- For 30% of patients there was no clear record of whether a response to a target behaviour had occurred.

Comment: failure to monitor response may lead to unnecessarily prolonged treatment or ineffective treatment with a high risk drug.

References

1. Banarjee S. The use of antipsychotic medication for people with dementia: A time for action. An independent report commissioned and funded by the Department of Health (England). October 2009. Available from: www.dh.gov.uk (Keyword Bannerjee) (Accessed January, 2010).
2. Opie J, Rosewarne R, O'Connor DW. The efficacy of psychosocial approaches to behaviour disorders in dementia; a systematic literature review. *Aust NZ J Psychiatry* 1999;33:789-99.
3. Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with dementia. A national clinical guideline. SIGN, 2006. Available from: www.sign.ac.uk/pdf/sign86.pdf (Accessed January, 2010).
4. Teri L, Logsdon RG, Uomoto J, McCurry SM. Behavioural treatment of depression in dementia patients: a controlled clinical trial. *J Gerontol B Psychol Sci Soc Sci* 1997;52(4):159-66.
5. Schneider LS, Dagerman K, Insel P. Efficacy and adverse effects of atypical antipsychotics for dementia: meta-analysis of randomised, placebo-controlled trials. *Am J Geriatr Psychiatry* 2006;14:191-210.
6. National Prescribing Service (NPS). The role of antipsychotics in managing BPSD. *Prescribing Practice Review* 37. NPS, 2007. Available from: www.nps.org.au (Accessed, January, 2010).
7. National Institute of Clinical Excellence (NICE). Dementia Guidelines, NICE 2006. Available from: www.nice.org.uk/cg42 (accessed January, 2010).
8. Ballard CG, Thomas A, Fossey J, et al. A 3-month, randomised, placebo-controlled, neuroleptic discontinuation study in 100 people with dementia: the neuropsychiatric inventory median cutoff is a predictor of clinical outcome. *J Clin Psychiatry* 2004;65:114-9.
9. Fossey J, Ballard C, Juszcak, et al. Effect of advanced psychosocial care on antipsychotic use in nursing home residents with severe dementia. *BMJ* 2006;332:756-61.



Safe prescribing of quetiapine and other antipsychotics in older people

THE USE OF ANTIPSYCHOTICS IN OLDER PEOPLE is associated with an increased risk of falls. Analysis of dispensing patterns for antipsychotics (September 2005 – May 2009) in people aged over 65 years, shows that use of the typical antipsychotics such as haloperidol has remained relatively stable, whereas there has been an increase in the use of the atypical antipsychotics (Figure 1).

Most, if not all, of this increase in atypical antipsychotic use can be attributed to increased volumes of quetiapine (Figure 2). In 2005 risperidone was the most dispensed atypical antipsychotic (56% of all atypical antipsychotics) compared with quetiapine (26%). The latest data indicates that they are now approximately equal on 40%.

What conclusions can be drawn from this analysis?

- The safety concerns about the use of antipsychotics in people with dementia have not reduced dispensing volumes in older people. This may be explained by the fact that antipsychotics, particularly quetiapine, are used in older people for indications other than BPSD.

- The increased volume of quetiapine may be attributed to its use as a hypnotic and sedative, in preference to a benzodiazepine. While there may be some therapeutic advantages of quetiapine over a benzodiazepine, quetiapine is not licensed for these indications and there are some safety concerns, especially postural hypotension and increased fall risk.

Safe prescribing of antipsychotics in older people

- Only prescribe for specific indications and review regularly. Avoid long-term use if possible.
- Start with a very low dose (e.g. 25 mg quetiapine) and titrate to effect carefully.
- Be vigilant for the possibility of excessive sedation and hypotension with antipsychotics, especially with quetiapine. Postural hypotension following the first dose can be sudden and profound, particularly in older people taking other hypotensive drugs and CNS depressants.
- Be aware of the possibility of drug interactions such as additive drowsiness and sedation with antihistamines, antidepressants and alcohol.

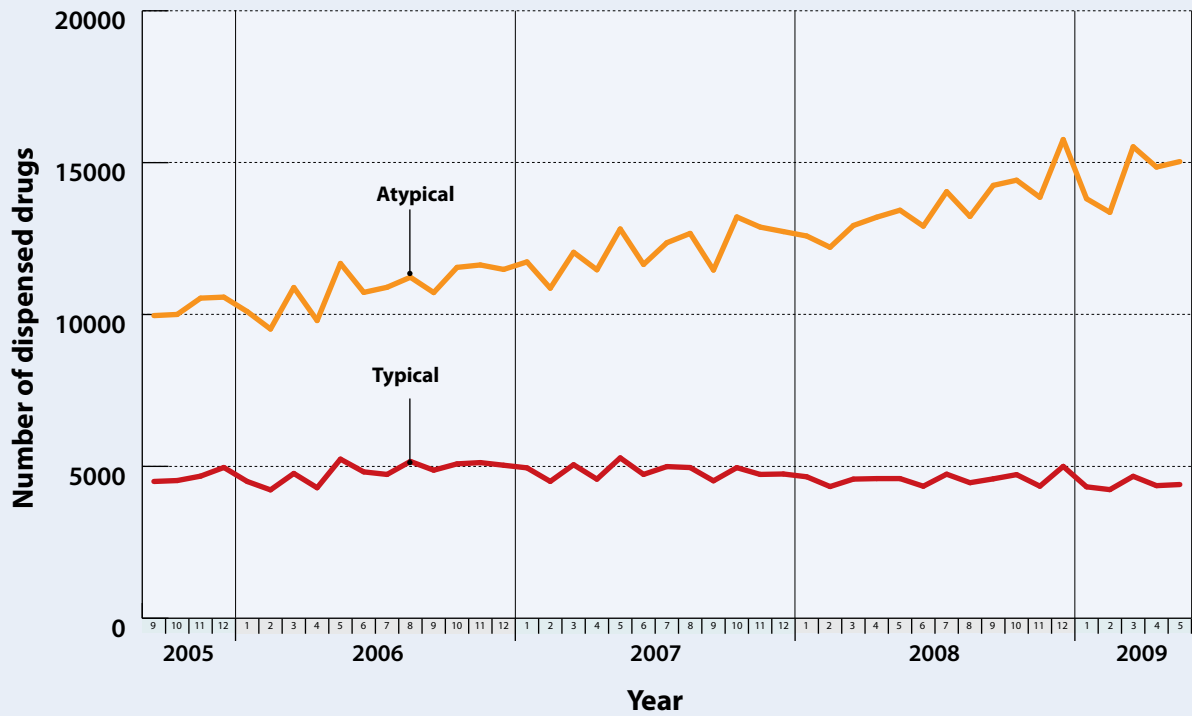


Figure 1: Dispensing of antipsychotics: Typical vs atypical

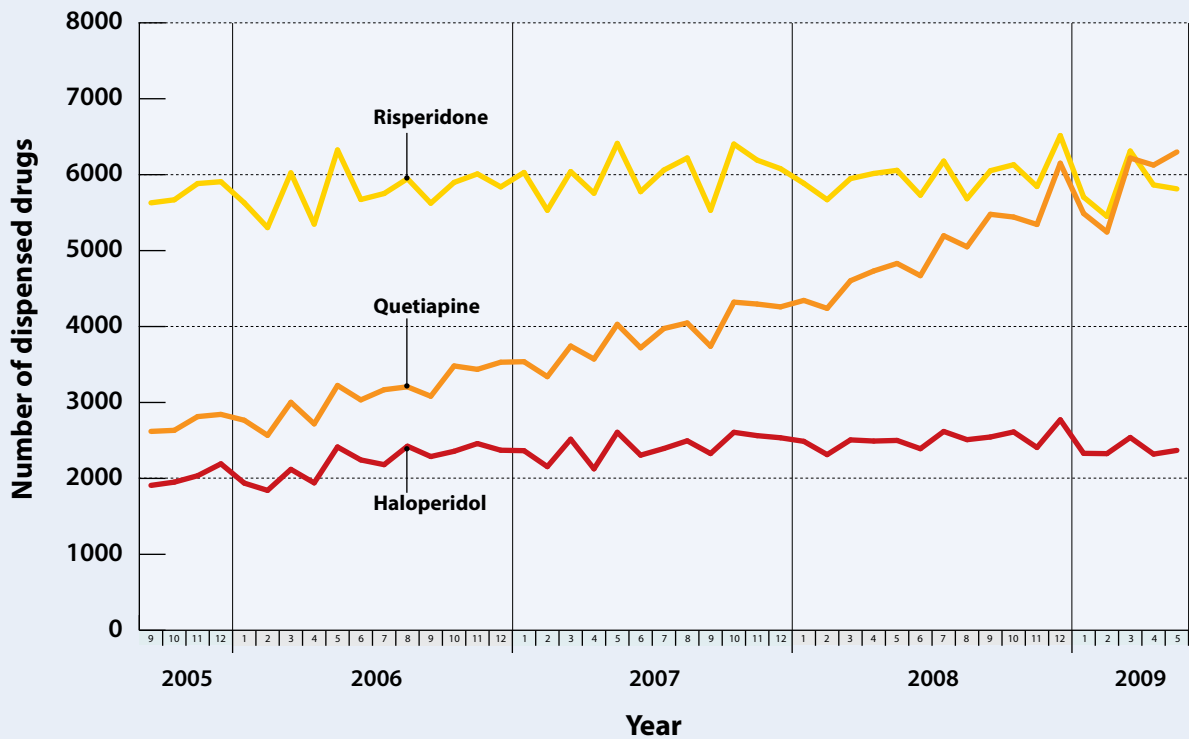


Figure 2: Dispensing of atypical antipsychotics