

## Psychotropic medication in the management of behaviours



### Background

The following information is intended to summarise the evidence around the use of various psychotropic medication in the management of what is known as behavioural and psychological symptoms of dementia (BPSD). It is not intended to be comprehensive, and restricts its scope to the more commonly prescribed medicines within an Australian context.

In addition to those medicines prescribed to help treat BPSD, it is important to also be aware of the commonly prescribed medications that might lead to an exacerbation of behaviours. In general, while it is true that any medication with central nervous system activity may precipitate or aggravate BPSD, the key drugs to avoid are those with anticholinergic activity. Cholinergic medications can improve cognition. Anticholinergics, therefore, cause increased confusion.

Anticholinergic medications tend to be of two types; those that are prescribed because they have anticholinergic properties, and those that are known to have anticholinergic side effects. Of the former, oxybutynin (Ditropan), benztropine (Cogentin) and benhexol (Artane) are the best known, while drugs with significant anticholinergic side effects include tricyclic antidepressants, frusemide, digoxin, opioid analgesics, salbutamol (Ventolin), ipratropium bromide (Atrovent), corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs).

### General Principles of Medication Management

1. Medications should only be used when behavioural interventions have been ineffective.
2. Tailor the choice of medication to the behaviour. Many behaviours, by their very nature, tend to be medication non-responsive. Such behaviours include wandering, shadowing, intrusiveness, inappropriate voiding, calling out and disrobing behaviours. Intuitively, the only way in which medication might decrease these behaviours is by sedating the person to the point where they are no longer able to engage in the behaviour. This is an inappropriate treatment goal outside of a palliative framework of care.
3. The use of antipsychotics should be limited to the treatment of severe aggression and psychosis. Whilst they are effective for treating agitation as well, they have more side effects than alternative medicines.

4. The natural history of BPSD is that there is a high rate of spontaneous remission within six months. Thus, if a behaviour has been settled for some months, a weaning of psychotropic medications is advised at that point.
5. In general, one medication at a time should be trialled, and increased according to effectiveness and tolerability. If any given medicine fails to improve behaviour, it should be ceased prior to another medicine being trialled.

## Pharmacotherapies available for BPSD

### Antipsychotics:

First-generation drugs (e.g. haloperidol, chlorpromazine) should generally not be used, despite being effective for the management of psychosis (delusions and hallucinations), agitation and aggression. They have very high rates of adverse effects in the elderly and should be avoided.

Second-generation drugs (e.g. risperidone, olanzapine, quetiapine) are better tolerated, but are no more effective than the first-generation medicines. Note that the only medicine available on the PBS for the management of BPSD is risperidone, for a period of up to 12 weeks.

Risperidone is effective for the management of psychosis, agitation and aggression. The effect size when used for agitation and aggression however, is small, and averages 0.2 across the seven studies that have been conducted (equating to about an 8% decrease in behaviour severity).

Antipsychotic use in this population is associated with significant harm. One study found that residents in aged care prescribed antipsychotics were 1.9-2.4 times more likely to have an adverse event requiring hospitalisation within 30 days of commencement. The rates of admission for patients prescribed these drugs in the community was increased between 3.2-3.8 times. (Arch. Int. Med. 2008;165:1050-1056).

### Antidepressants:

There have been only six randomised controlled trials examining the effectiveness of antidepressants in BPSD. Of these, positive findings were observed only for citalopram, specifically for its benefits on agitation and lability.

It should be noted that there are no agreed diagnostic criteria for depression in severe dementia (the Cornell scale has not been validated in those with an MMSE<10). It is thus possible that some of those diagnosed with BPSD in these trials may well have been depressed (with depression unrecognised and manifesting as 'behaviour'). If this is the case a response to citalopram is unsurprising.

This may explain why most current pharmacotherapy guidelines for the management of BPSD suggest a trial of an SSRI antidepressant in the first instance.

The literature examining antidepressant efficacy for the treatment of depression in dementia is contradictory. The largest of these trials (Banerjee et al. Lancet 2011 Jul 30;378 (9789):403-11) found no differences in outcomes between those treated with sertraline, mirtazapine and 'normal care' after 36 weeks. Severely depressed patients were excluded from this and other studies, however, and expert opinion still supports the use of antidepressants in this group.

Tricyclic antidepressants should be avoided due to their high anticholinergic side effect load.

### Benzodiazepines:

These medicines have been shown to be effective for agitated behaviours such as insomnia, anxiety, tension and irritability.

Tolerance can develop over time, leading to loss of efficacy. Side effects include excessive sedation, worsening confusion, ataxia and falls.

Short-acting medicines with no secondary metabolites (e.g. oxazepam, temazepam) are the medicines of choice.

## **Cholinesterase inhibitors:**

A meta-analysis of 29 randomised controlled trials found these medicines to have modest efficacy in BPSD for those with mild to moderate dementia. There appear to be no differences in efficacy between the available drugs. There is no convincing evidence to support their use in more severe dementia.

## **Memantine:**

A Cochrane review found memantine to have a small effect on cognition and function in moderate to severe Alzheimer's disease.

Fewer patients on memantine develop agitation compared to those on placebo, suggesting a direct anxiolytic effect. The tolerability of the drug is similar to placebo.

Two community-based randomised controlled trials have shown beneficial effects on agitation and aggression, but these findings cannot necessarily be generalised to nursing home populations

## **Anticonvulsants:**

A Cochrane review on the efficacy of valproate in treating BPSD found that low doses were ineffective, whilst higher doses were poorly tolerated, causing unacceptable side effects. The review concluded that current evidence does not support its use.

The literature around carbamazepine is inconclusive (Int. Psychoger. 2008;20;2:293-308) and has been summarised by the National Institute for Clinical Excellence (NICE) in the UK.

## **General notes**

Much of the evidence around medication use in BPSD is of poor quality, with most studies beset by methodological problems. BPSD is a heterogeneous problem that is caused by the complex interplay of biological, psychological and social factors over time. It is thus not surprising that the evidence for the usefulness of ANY medication in BPSD is limited.

In those instances where there is robust evidence of efficacy, effect sizes are small.

Those medicines for which there is good evidence have major problems with side effects.

**Dementia Support Australia can provide advice and medical reviews by aged psychiatry and geriatrician with the agreement of the general practitioner.**

This resource material is informed by literature and associate practice evidence. This guidance should be applied within your organisations policies and procedures.