Dementia: withdrawal of antipsychotic drugs in people with behavioural and neuropsychiatric symptoms

A Cochrane review has evaluated the effect of withdrawing treatment with antipsychotic drugs prescribed for behavioural and neuropsychiatric symptoms in people with dementia. It concluded that these can be withdrawn without detrimental effects on behaviour in many people. This review is consistent with the NICE/SCIE clinical guideline on dementia and the Alzheimer’s Society best practice guide.

Overview and current advice

The harms and limited benefits of using antipsychotic drugs for treating dementia in people who exhibit challenging behaviours are well recognised. They have been the subject of several previous reviews and MHRA warnings, collated in the May 2012 edition of Drug Safety Update.

The NICE/Social Care Institute for Excellence (SCIE) guideline Dementia: supporting people with dementia and their carers in health and social care advises against the use of any antipsychotics for non-cognitive symptoms or challenging behaviour of dementia unless the person is severely distressed or there is an immediate risk of harm to them or others. Any use of antipsychotics should include a full discussion with the person and carers about the possible benefits and risks of treatment.

In July 2011, a best practice guide, Optimising treatment and care for people with behavioural and psychological symptoms of dementia, was produced by the Alzheimer’s Society and endorsed by the Department of Health. These resources build on the NICE/SCIE guideline and include strategies to reduce inappropriate prescribing of antipsychotics. The best practice guide outlines care pathways around preventing symptoms from developing before medication needs to be prescribed, and reviewing antipsychotic prescriptions with a view to discontinuing these where possible.

Carers looking after people with dementia who are taking antipsychotic drugs to manage behavioural and psychological symptoms are sometimes, understandably, reluctant to consider withdrawal of these drugs, for fear that these symptoms will deteriorate. A Cochrane review has recently been published which assessed the risks, benefits and feasibility of antipsychotic drug withdrawal in such people.
Low-dose antipsychotic prescribing in people with dementia is one of the therapeutic areas in the Key therapeutic topics - Medicines management options for local implementation document produced to support the QIPP medicines use and procurement work stream. See also the NICE quality standard on dementia, the NICE Evidence topic page on dementia, and the NICE Pathway, which brings together all related NICE guidance and associated products on dementia in a set of interactive topic-based diagrams.

New evidence

A Cochrane review has evaluated the withdrawal of antipsychotic drugs prescribed for behavioural and neuropsychiatric symptoms of dementia\(^3\). It included 9 placebo-controlled, randomised controlled trials (RCTs), 7 of which were carried out exclusively in nursing homes, which compared an antipsychotic withdrawal strategy with the continuation of antipsychotics in 606 people with dementia.

The included trials were very different with regard to study participants (such as the severity of dementia), types and dosages of antipsychotics used before withdrawal, methods of withdrawal, outcomes and time of assessment. The antipsychotics used (for at least 3 months) before withdrawal included chlorpromazine, haloperidol, olanzapine, risperidone, thioridazine, or trifluoperazine in different dosages, and both abrupt and gradual withdrawal schedules were used.

The primary efficacy outcomes were success of withdrawal from antipsychotics, which was defined as no drop out from the trial due to worsening neuropsychiatric symptoms or relapse to antipsychotic drug use, or behavioural or neuropsychiatric symptoms measured with an appropriate scale. However, because the included trials used different measures, these were difficult to compare.

In 7 of the 9 trials there was no overall statistically significant difference between groups on the primary outcomes. Also, in the only outcome that could be pooled (full neuropsychiatric inventory [NPI] score, possible score range 1–144), there was no statistically significant difference between people withdrawn from and those continuing antipsychotics at 3 months (mean difference \(\text{−1.49, 95% confidence interval (CI) −5.39 to 2.40}\); 2 RCTs, \(n=265\)).

However, 2 RCTs included people with psychosis and agitation that had responded to antipsychotics. In these patients, there was a shorter time to relapse after haloperidol discontinuation (actual difference not stated, \(p=0.04, n=20\)) and an increased risk of relapse in the first 16 weeks after risperidone discontinuation compared with continuing the drug (24 of 40 [60%] versus 23 of 70 [33%], hazard ratio 1.94, 95% CI 1.09 to 3.45, \(p=0.02\)). In the 2 RCTs where NPI score could be pooled, there was also evidence of statistically significant behavioural deterioration in people with more severe baseline neuropsychiatric symptoms who were withdrawn from antipsychotics.

Although the methodological quality of the included trials was assessed as generally good, all the included studies had problems recruiting enough frail older people, and the statistical power of the studies was low. Most of the included trials were not powered to detect clinically important differences between groups, and adverse events were not systematically assessed. Long-term follow-up from 1 RCT raised concerns about a possible increase in mortality in people continuing antipsychotics for up to 3 years. However, this result needs to be interpreted cautiously.

From their findings, the authors conclude that antipsychotic medication can be withdrawn from many people with dementia and neuropsychiatric symptoms without detrimental effects on their behaviour, and discontinuation programmes could be incorporated into routine practice. Caution, is however, required in people with more severe neuropsychiatric symptoms and in people with psychosis and agitation who responded well to antipsychotics before.
Commentary

Commentary provided by the Medicines and Prescribing Centre

Despite the limitations with this Cochrane review, in particular differences between the included trials (which prevented pooling of data) and the low statistical power of the included studies, its findings support national strategies to reduce inappropriate prescribing of antipsychotics in people with dementia.

The best practice guide, Optimising treatment and care for people with behavioural and psychological symptoms of dementia, states that, 'While atypical antipsychotics do confer modest benefits in treating aggression and psychosis over 6 to 12 weeks, they are associated with a number of major adverse outcomes and side effects including sedation, parkinsonism, gait disturbance, dehydration, falls, chest infections, accelerated cognitive decline, stroke and death. It was estimated in a report for the Department of Health that 180,000 people with dementia are receiving antipsychotic drugs in the UK. The consequences include 1,800 additional strokes and 1,600 additional deaths each year in the UK among people with dementia.'

As is discussed in the key therapeutic topic Low-dose antipsychotic prescribing in people with dementia, the National dementia and antipsychotic prescribing audit suggests that there has been an encouraging overall reduction in the proportion of people with dementia being prescribed antipsychotics in recent years. Based on data from 46% of GP practices across England, the audit found that the number of people newly diagnosed each year with dementia increased by 68% in relative terms from 2006 to 2011. However, there was a decrease of 10.25 percentage points in the number of people with dementia receiving prescriptions for antipsychotic medication over that time (from 17.05% in 2006 to 6.80% of people in 2011, a 60% reduction in relative terms). Nevertheless, there was still considerable variation in the percentage of people diagnosed with dementia prescribed an antipsychotic.

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References


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