Withdrawal versus continuation of chronic antipsychotic drugs for behavioural and psychological symptoms in older people with dementia

Objectives
Antipsychotic agents are often used to treat neuropsychiatric symptoms (NPS) in dementia, although the literature is sceptical about their long-term use for this indication.

Although regular attempts to withdraw these drugs are recommended, physicians, nurses and families of older people with dementia are often reluctant to try to stop antipsychotics, fearing deterioration of NPS.

The authors evaluated whether withdrawal of antipsychotic agents is successful in older people with dementia in community or nursing home settings.

Search and selection strategy
The authors searched ALOIS, the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG), The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL, Lilacs and clinical trials registries.

Randomised, placebo-controlled trials comparing an antipsychotic withdrawal strategy to continuation of antipsychotics in people with dementia were selected. Review authors independently assessed trials for inclusion, rated their risk of bias and extracted data.

Main results
The authors included nine trials with 606 randomised participants. Seven trials were conducted in nursing homes, one trial in an outpatient setting and one in both settings. In these trials, different types of antipsychotics prescribed at different doses were withdrawn. Both abrupt and gradual withdrawal schedules were used.

The risk of bias of the included studies was generally low regarding blinding and outcome reporting and unclear for randomisation procedures and recruitment of participants.

There was a wide variety of outcome measures. Our primary efficacy outcomes were success of withdrawal, i.e., remaining in study off antipsychotics, and NPS.

Eight of nine trials reported no overall significant difference between groups on the primary outcomes, although in one pilot study of people with psychosis and agitation that had responded to haloperidol, time to relapse was significantly shorter in the discontinuation group (p=0.04).

The ninth trial included people with psychosis or agitation who had responded well to risperidone therapy for four to eight months and reported that discontinuation led to an increased risk of relapse.

The only outcome that could be pooled was the full Neuropsychiatric Inventory (NPI) score, used in two studies. For this outcome there was no significant difference between people withdrawn from and those continuing on antipsychotics at three months (mean difference: -1.49, 95% CI -5.39 to 2.40).

In both studies, there was evidence of significant behavioural deterioration in people with more severe baseline NPS who were withdrawn from antipsychotics.

Individual studies did not report significant differences between groups on any other outcome except one trial that found a significant difference in a measure of verbal fluency, favouring discontinuation. Most trials lacked power to detect clinically important differences between groups.

Adverse events were not systematically assessed. In one trial there was a nonsignificant increase in mortality in people who continued antipsychotic treatment (5–8 per cent greater than placebo, depending on the population analysed, measured at 12 months).

Authors’ conclusions
The findings suggest that many older people with Alzheimer’s dementia and NPS can be withdrawn from chronic antipsychotic medication without detrimental effects on their behaviour.

It remains uncertain whether withdrawal is beneficial for cognition or psychomotor status, but the results of this review suggest that discontinuation programmes could be incorporated into routine practice.

However, two studies of people whose agitation or psychosis had previously responded well to antipsychotic treatment found an increased risk of relapse or shorter time to relapse after discontinuation.

Two other studies suggest that people with more severe NPS at baseline could benefit from continuing their antipsychotic medication. In these people, withdrawal might not be recommended.

Citation