

Antipsychotics can be withdrawn from many older people with dementia, though caution is needed for people with more severe neuropsychiatric symptoms

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QUESTION

Question: Is the withdrawal of antipsychotic medication in older people with dementia and neuropsychiatric symptoms (NPS) feasible, safe and effective?

Outcomes: *Primary outcomes:* success of withdrawal strategy, defined as remaining in the trial off antipsychotic medication (no dropout due to worsening NPS or relapse to antipsychotic use during the trial); behavioural and psychological symptoms, especially agitation, aggression and psychotic symptoms; withdrawal symptoms (including autonomic and behavioural symptoms) and adverse effects of antipsychotics. *Secondary outcomes:* cognitive function; quality of life (participants and carers); use of physical restraint; and mortality.

METHODS

Design: Systematic review and meta-analysis.

Data sources: The Specialised Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG) and ALOIS, which is maintained by the Dementia Group and includes studies identified from CENTRAL, MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS, clinical trials registries and grey literature sources; search dates February 2009 to November 2012.

Study selection and analysis: *Inclusions:* Randomised placebo-controlled trials comparing an antipsychotic withdrawal strategy (either abrupt or tapered) with medication continuation, in older people (≥ 65 years) with dementia under primary care or living in a nursing home. Non-placebo-controlled trials were included if the outcome assessors were blinded. All types and subtypes of dementia of any severity were included regardless of the method of diagnosis.

MAIN RESULTS

Nine studies ($n=606$) met inclusion criteria. Seven of the trials were conducted in a nursing home, one in an outpatient setting and one in both settings. The type and dose of antipsychotic withdrawn varied across the nine studies.

Three studies used an abrupt withdrawal schedule, four studies used a tapering approach and two studies used an abrupt approach for the majority of participants and tapered the withdrawal for individuals taking a baseline dose of ≥ 50 mg chlorpromazine or ≥ 2 mg risperidone. Six of the studies provided data on antipsychotic withdrawal success rate. Four of these trials reported no significant difference in dropout rates due to worsening NPS; while two studies in people whose agitation or psychosis had responded to haloperidol or risperidone found significantly higher relapse rates in the antipsychotic withdrawal groups compared to the continuation groups. Six studies assessed the effect of antipsychotic withdrawal on behavioural and psychological symptoms; none of these trials found withdrawal to have a significant effect on these outcomes. Owing to the variation in symptom outcome measures, meta-analysis was only performed for two studies ($n=90$) that measured behavioural outcomes at 3 months using the neuropsychiatric inventory (NPI). Antipsychotic withdrawal had no effect on behaviour in these studies (pooled mean difference in NPI scores -1.49 , 95% CI -5.39 to $+2.40$). No studies reported withdrawal symptoms. Five studies reported adverse events of antipsychotics, and found no significant differences between withdrawal and continuation groups. All six studies assessing cognitive function found no significant effect of withdrawal on either the mini mental state examination or other measures. One study found that antipsychotic withdrawal had no significant effect on the quality of life, and one study found no significant effect on the use of physical restraint.

CONCLUSIONS

Overall, for most people with dementia and neuropsychiatric symptoms, antipsychotic withdrawal has no detrimental effect on behaviour, psychological or cognitive outcomes. However, two trials in people who had previously responded to antipsychotics found increased rates of relapse following withdrawal.

ABSTRACTED FROM

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Antipsychotic drugs are commonly prescribed to manage various behavioural and psychological symptoms of dementia (BPSD). Despite their popular use in this setting, accumulating evidence has linked antipsychotic drug use to increased overall mortality among older adults with dementia. As a result, regular attempts to withdraw these drugs have been recommended.

Declercq and colleagues review the evidence from nine relatively small clinical trials in which people with BPSD were randomised to either an antipsychotic withdrawal strategy or continuation of antipsychotic treatment. Most trials found no significant differences in outcomes between the withdrawal and continuation groups, with caveats from two trials. First, antipsychotic withdrawal might lead to worsening BPSD

if attempted too soon after a good response to treatment. Second, higher relapse rates were observed in people who had more severe behavioural symptoms just prior to the withdrawal attempt.

This review reminds us to consider the potential of drug discontinuation trials, which remain uncommon, but may become more popular in the future because of the significant medication burden of frail older adults and concerns about the shifting balance of benefit to risk for many medications as people age. For example, recent trials have evaluated the discontinuation of antidepressant drugs and cholinesterase inhibitors in people with dementia.^{1 2}

Clinicians should consider that tapered withdrawal may be preferable to sudden discontinuation in patients with dementia, and attempts at

antipsychotic withdrawal in patients who have had a recent good response to treatment or who have continuing severe BPSD should be avoided, as withdrawal is less likely to succeed in these circumstances. Decision-making related to antipsychotic drug treatment in dementia remains challenging, and requires a thoughtful approach that balances the risk of relapse with discontinuation against the risk of adverse events with ongoing antipsychotic treatment.

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