FPIN's Help Desk Answers

Short-Term Antipsychotics for Alzheimer Disease

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Clinical Question

Do patients with Alzheimer disease who are treated with short-term antipsychotics have a higher mortality rate than those not taking antipsychotics?

Evidence-Based Answer

Physicians should consider not using antipsychotics in patients with dementia. (Strength of Recommendation: A, based on a meta-analysis of randomized controlled trials [RCTs] and a cohort study.) Patients with dementia, including Alzheimer disease, who are treated with antipsychotics for any length of time have a higher mortality rate than those not taking antipsychotics.

Evidence Summary

A 2005 systematic review and meta-analysis of 15 RCTs of 10 to 26 weeks' duration compared mortality in patients 56 to 99 years of age who received atypical antipsychotics or placebo.[1] Patients had Alzheimer disease, vascular dementia, mixed dementia, or primary dementia. Overall, 87% of patients had Alzheimer disease. Subgroup analysis did not find heterogeneity between trials of patients with Alzheimer disease and higher cognitive function (Mini-Mental State Examination score greater than 10) vs. lower cognitive function. Of the 5,110 patients, 1,757 were randomized to placebo and 3,353 were randomized to an atypical antipsychotic, including aripiprazole (Abilify), 2 to 15 mg per day; risperidone (Risperdal), 0.5 to 4 mg per day; quetiapine (Seroquel), 50 to 600 mg per day; and olanzapine (Zyprexa), 1 to 15 mg per day. In pooled analysis of all 15 RCTs, death was more common among patients receiving atypical antipsychotics (odds ratio = 1.5; 95% confidence interval [CI], 1.1 to 2.2; number needed to harm [NNH] = 83). Patients with Alzheimer disease were not analyzed separately from those with other causes of dementia.

A 2014 retrospective cohort study investigated short- and long-term mortality risk associated with antipsychotic use in outpatients 65 years and older who had dementia (n = 26,940).[2] Risk was assessed over multiple timeframes and for multiple antipsychotics. Patients had records in the Norwegian Prescription Database and were assumed to have dementia based on treatment with at least one antidementia drug (memantine [Namenda], donepezil [Aricept], rivastigmine [Exelon], or galantamine [Razadyne]). The antipsychotic group (n = 8,214) had also received a prescription for risperidone, olanzapine, quetiapine, levomepromazine (not available in the United States), perphenazine, prochlorperazine, haloperidol, zuclopenthixol (not available in the United States), or chlorprothixene (Taractan), whereas the control group (n = 18,726) was receiving other psychotropic drugs, including

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antidepressants, benzodiazepines, lithium, and anticonvulsants. Survival analyses were adjusted for age, sex, mean daily dosage, and medical conditions. Compared with use of other psychotropic drugs, antipsychotic use increased mortality risk at 30 days (hazard ratio = 2.1; 95% CI, 1.6 to 2.9; NNH = 89) and two to six years (hazard ratio = 1.7; 95% CI, 1.6 to 1.9; NNH = 11). The percentage of patients with Alzheimer disease vs. other types of dementia was not reported.

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References

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2. Langballe EM, Engdahl B, Nordeng H, Ballard C, Aarsland D, Selbæk G. Short- and long-term mortality risk associated with the use of antipsychotics among 26,940 dementia outpatients: a population-based study. *Am J Geriatr Psychiatry*. 2014;22(4):321-331. ■