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Antidepressants for agitation and psychosis in dementia

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Abstract

Background: Agitation and psychosis are common among older adults with dementia and are challenging to manage. At the present time, little is known about the efficacy and safety of antidepressant medications when used to treat these symptoms.

Objectives: To assess the safety and efficacy of antidepressants in treating psychosis and agitation in older adults with Alzheimer's disease, vascular, or mixed dementia.

Search strategy: We searched the Cochrane Dementia and Cognitive Improvement Group's Specialized Register which included Cochrane Central Register of Controlled Trials (The Cochrane Library 2009, Issue 3), MEDLINE (January 1950 to October 2009), EMBASE (1980 - October 2009), CINAHL (all dates - October 2009) and PsycINFO (1806 to October 2009).

Selection criteria: Randomized, controlled trials of antidepressants (selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, trazodone, and other antidepressants), compared to either placebo or comparator medications (typical or atypical antipsychotics, anticonvulsants, benzodiazepines, cholinesterase inhibitors, memantine or other medications) for treatment of agitation or psychosis in older adults with dementia.

Data collection and analysis: Two authors independently assessed trial quality and extracted trial data. We collected information on efficacy as measured by dementia neuropsychiatric symptom rating scales and adverse effects. Study authors were contacted for additional information.

Main results: Nine trials including a total of 692 individuals were included in the review. Five studies compared SSRIs to placebo and two studies were combined in a meta-analysis for the outcome of change in Cohen-Mansfield Agitation Inventory (CMAI) scores. There was a significant difference between antidepressants and placebo on measures of agitation as reported on the change in CMAI total score (mean difference (MD), -0.89, 95% CI, -1.22 to -0.57) although the results were heavily weighted by one large study. There were no significant differences in change in behavioral symptoms of dementia for SSRIs compared to placebo in the one study that reported on changes in the Neuropsychiatric Inventory and Behavioral Pathology in Dementia scales. One study comparing citalopram to placebo found a significant difference in NPS as measured on the Neurobehavioral Rating Scale (NBRS) after controlling for baseline severity NBRS score although the unadjusted mean difference was not statistically significant (MD - 7.70, 95% CI: -16.57 to 1.17). There was no difference in the rates of trial withdrawals due to adverse events for SSRIs compared to placebo for four studies reporting this outcome (relative risk (RR), 1.07, 95% CI: 0.55 to 2.11) or in the number of trial withdrawals due to any cause in the three studies reporting this outcome (RR, 0.91, 95% CI, 0.65 to 1.26). One study compared the SSRI citalopram to the atypical antipsychotic risperidone and found no

difference in NBR scores, trial withdrawals due to any cause or trial withdrawals due to adverse events although the rates of adverse events as measured on the UKU side effect scale total score were lower for citalopram (MD -2.82, 95% CI: -4.94 to -0.70). Three studies compared SSRIs to typical antipsychotics. In meta-analysis of two studies there was no statistically significant differences in changes in CMAI total scores (MD, 4.66, 95% CI: -3.58 to 12.90). There was also no difference in trial withdrawals due to any cause or due to adverse events for SSRIs compared to typical antipsychotics. One study of trazodone compared to placebo did not find any significant difference in change in CMAI total scores (MD, 5.18, 95% CI, -2.86 to 13.22) or trial withdrawals due to any cause (RR, 1.06, 95% CI, 0.54 to 2.09). Two studies comparing trazodone to haloperidol also failed to detect any difference in change in CMAI total scores (MD, 3.28, 95% CI, -3.28 to 9.85) or trial withdrawals due to any cause (RR, 0.79, 95% CI, 0.43 to 1.46).

Authors' conclusions: Currently there are relatively few studies of antidepressants for the treatment of agitation and psychosis in dementia. The SSRIs sertraline and citalopram were associated with a reduction in symptoms of agitation when compared to placebo in two studies. Both SSRIs and trazodone appear to be tolerated reasonably well when compared to placebo, typical antipsychotics and atypical antipsychotics. Future studies involving more subjects are required to determine if SSRIs, trazodone, or other antidepressants are safe and effective treatments for agitation and psychosis in dementia.

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