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[Intervention Review]

# Antipsychotics for treatment of delirium in hospitalised non-ICU patients

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## ABSTRACT

### Background

Guidelines suggest limited and cautious use of antipsychotics for treatment of delirium where nonpharmacological interventions have failed and symptoms remain distressing or dangerous, or both. It is unclear how well these recommendations are supported by current evidence.

### Objectives

Our primary objective was to assess the efficacy of antipsychotics versus nonantipsychotics or placebo on the duration of delirium in hospitalised adults. Our secondary objectives were to compare the efficacy of: 1) antipsychotics versus nonantipsychotics or placebo on delirium severity and resolution, mortality, hospital length of stay, discharge disposition, health-related quality of life, and adverse effects; and 2) atypical vs. typical antipsychotics for reducing delirium duration, severity, and resolution, hospital mortality and length of stay, discharge disposition, health-related quality of life, and adverse effects.

### Search methods

We searched MEDLINE, Embase, Cochrane EBM Reviews, CINAHL, Thomson Reuters Web of Science and the Latin American and Caribbean Health Sciences Literature (LILACS) from their respective inception dates until July 2017. We also searched the Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment Database, Web of Science ISI Proceedings, and other grey literature.

### Selection criteria

We included randomised and quasi-randomised trials comparing 1) antipsychotics to nonantipsychotics or placebo and 2) typical to atypical antipsychotics for the treatment of delirium in adult hospitalised (but not critically ill) patients.

## Data collection and analysis

We examined titles and abstracts of identified studies to determine eligibility. We extracted data independently in duplicate. Disagreements were settled by further discussion and consensus. We used risk ratios (RR) with 95% confidence intervals (CI) as a measure of treatment effect for dichotomous outcomes, and between-group standardised mean differences (SMD) with 95% CI for continuous outcomes.

## Main results

We included nine trials that recruited 727 participants. Four of the nine trials included a comparison of an antipsychotic to a nonantipsychotic drug or placebo and seven included a comparison of a typical to an atypical antipsychotic. The study populations included hospitalised medical, surgical, and palliative patients.

No trial reported on duration of delirium. Antipsychotic treatment did not reduce delirium severity compared to nonantipsychotic drugs (standard mean difference (SMD) -1.08, 95% CI -2.55 to 0.39; four studies; 494 participants; very low-quality evidence); nor was there a difference between typical and atypical antipsychotics (SMD -0.17, 95% CI -0.37 to 0.02; seven studies; 542 participants; low-quality evidence). There was no evidence antipsychotics resolved delirium symptoms compared to nonantipsychotic drug regimens (RR 0.95, 95% CI 0.30 to 2.98; three studies; 247 participants; very low-quality evidence); nor was there a difference between typical and atypical antipsychotics (RR 1.10, 95% CI 0.79 to 1.52; five studies; 349 participants; low-quality evidence). The pooled results indicated that antipsychotics did not alter mortality compared to nonantipsychotic regimens (RR 1.29, 95% CI 0.73 to 2.27; three studies; 319 participants; low-quality evidence) nor was there a difference between typical and atypical antipsychotics (RR 1.71, 95% CI 0.82 to 3.35; four studies; 342 participants; low-quality evidence).

No trial reported on hospital length of stay, hospital discharge disposition, or health-related quality of life. Adverse event reporting was limited and measured with inconsistent methods; in those reporting events, the number of events were low. No trial reported on physical restraint use, long-term cognitive outcomes, cerebrovascular events, or QTc prolongation (i.e. increased time in the heart's electrical cycle). Only one trial reported on arrhythmias and seizures, with no difference between typical or atypical antipsychotics. We found antipsychotics did not have a higher risk of extrapyramidal symptoms (EPS) compared to nonantipsychotic drugs (RR 1.70, 95% CI 0.04 to 65.57; three studies; 247 participants; very-low quality evidence); pooled results showed no increased risk of EPS with typical antipsychotics compared to atypical antipsychotics (RR 12.16, 95% CI 0.55 to 269.52; two studies; 198 participants; very low-quality evidence).

## Authors' conclusions

There were no reported data to determine whether antipsychotics altered the duration of delirium, length of hospital stay, discharge disposition, or health-related quality of life as studies did not report on these outcomes. From the poor quality data available, we found antipsychotics did not reduce delirium severity, resolve symptoms, or alter mortality. Adverse effects were poorly or rarely reported in the trials. Extrapyramidal symptoms were not more frequent with antipsychotics compared to nonantipsychotic drug regimens, and no different for typical compared to atypical antipsychotics.

## PLAIN LANGUAGE SUMMARY

### Antipsychotics to treat delirium in hospitalised patients, not including those in intensive care units

#### Review question

We reviewed the evidence for the effectiveness and safety of antipsychotics for treatment of delirium in hospitalised patients, not including those in intensive care units (specialised wards for caring for very sick patients).

#### Background

Delirium is a public health concern as it is a new onset confused state that increases the amount of time patients spend in the hospital, as well as their chance of dying. Guidelines recommendations include reversal of any potential medical or drug triggers that may be contributing to delirium. If delirium symptoms persist and are distressing or dangerous, an antipsychotic drug may be prescribed for a short time. Antipsychotic drugs, also known as tranquillizers, are mainly used to treat psychosis (e.g. hallucinations). There are two types of antipsychotics: first generation or typical antipsychotics (e.g. haloperidol) and second generation or atypical antipsychotics (e.g. quetiapine). Both groups of antipsychotics block the brain's dopamine receptor pathways but atypical antipsychotics also act on serotonin receptors. Atypical antipsychotics are also noted to be effective for treating both the positive symptoms (e.g. hallucinations) as well as the negative symptoms (e.g. emotional withdrawal) of psychosis. We need to understand if antipsychotics shorten the course of delirium or reduce symptoms or if they cause more harm. Therefore, we updated the existing Cochrane Review from 2007.

#### Study characteristics

We found nine studies with 727 participants testing antipsychotics for delirium treatment; four trials compared an antipsychotic to another drug class or placebo and seven of the nine trials compared a typical antipsychotic to an atypical antipsychotic.

#### Key findings

We found no evidence to support or refute the suggestion that antipsychotics shorten the course of delirium in hospitalised patients. Based on the available studies, antipsychotics do not reduce the severity of delirium or resolve symptoms compared to nonantipsychotic drugs or placebo or lower the risk of dying. We found no evidence to support or refute the suggestion that antipsychotics shorten hospital length of stay or improve health-related quality of life. Side effects were rarely reported in the studies.

**Quality of the Evidence**

It is important to note many clinically relevant outcomes were not reported in the studies and the overall quality of the available evidence was poor.

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