Antipsychotic agents for the treatment of substance use disorders in patients with and without comorbid psychosis

CRD summary
The review objective appeared to be to determine the effectiveness of atypical antipsychotic agents in treating substance use disorders in people with and without comorbid psychosis. The authors concluding that atypical antipsychotics may decrease alcohol and drug disorders in patients with comorbid psychosis. Due to uncertain study quality and variability and poor review process reporting, the conclusions should be interpreted with caution.

Authors' objectives
The authors appeared to determine the effectiveness of atypical antipsychotic agents in treating substance use disorders in people with and without comorbid psychosis.

Searching
The authors searched PubMed and EMBASE for relevant studies published between January 1962 and June 2010. Search terms were reported. Reference lists were searched to identify further studies.

Study selection
Randomised blinded placebo-placebo controlled studies or case-control studies with a duration of at least four weeks that assessed antipsychotic treatment in patients with substance use disorders were eligible for inclusion. Only randomised studies were considered for patients without psychosis (defined as schizophrenia, schizoaffective disorder and bipolar disorder). Two or more antipsychotic treatments had to be compared in studies of patients with psychosis. Case reports, open-label studies and cross-sectional designs were excluded. Eligible outcomes had to measure craving, alcohol-drug use and/or relapse.

Within included trials, length of follow-up ranged from six to 144 weeks. Within comorbid psychosis studies, almost all focused on alcohol, stimulant and tobacco disorders. Most patients had schizophrenia. Comorbid psychosis regimens included clozapine, olanzapine, risperidone, long-acting risperidone, quetiapine, zuclopenthixol depot and haloperidol. Within non-comorbid psychosis studies, all studies were either of stimulant or alcohol substance use disorder. Non-comorbid psychosis regimens included flupenthixol decanoate, tiapride, amisulpride, olanzapine, quetiapine, aripiprazole, risperidone, long-acting risperidone and flupenthixol decanoate (dosages were reported for most trials).

The number of reviewers who performed the study selection was not reported.

Assessment of study quality
No detailed quality assessment of included studies was reported.

Data extraction
The direction of effect was presented for various outcomes of interest.

The number of reviewers who performed data extraction was not stated.

Methods of synthesis
A narrative synthesis was conducted due to the clinical heterogeneity of the included studies.

Results of the review
Forty-three studies (n=3,617, range 12 to 362) were included in the review: 23 comorbid psychosis studies and 20 non-comorbid psychosis studies. All non-comorbid psychosis studies were randomised and double-blinded and all except one were placebo-controlled. Thirteen of the comorbid psychosis studies were randomised, 10 were double-blinded and two were placebo-controlled.
Comorbid psychosis patients: Four studies demonstrated that clozapine led to substantial improvements in substance use disorder outcomes with alcohol use disorders. Seven studies were taken to indicate that other types of atypical antipsychotics (including quetiapine, olanzapine and risperidone) might lead to improvements in alcohol and illegal drug use. Four studies suggested atypical antipsychotics reduced cravings in patients with stimulant use disorders; two studies showed no effect in this group.

Non-comorbid psychosis patients: Two studies found aripiprazole to be associated with improvements in alcohol dependence. Five studies found antipsychotic agents to be associated with increased relapse rates in patients with alcohol use disorders. Three studies found atypical antipsychotics to be associated with improvements in subgroups of people with alcohol use disorder. Five studies demonstrated that antipsychotics did not improve and may even have aggravated dependence in patients with stimulant use disorder.

Authors' conclusions
Studies of patients with comorbid psychosis suggested that atypical antipsychotics, especially clozapine, may decrease alcohol and drug use disorders. Studies of patients without comorbid psychosis suggested that atypical antipsychotics be beneficial in treating alcohol dependence in some alcoholic subpopulations, but may not be effective in treating stimulant dependence and aggravated the condition in some cases.

CRD commentary
This review addressed an unclear review question using clearly reported study selection criteria. Only two databases were searched, which increased risks of publication bias and missing studies. Search terms were reported. No assessment of publication bias was reported and so publication bias could not be ruled out. Many details from the included studies were reported and these assisted in the assessment of generalisability. The included study designs appeared to contain low risks of bias. The number of reviewers involved at each stage of the review process was not reported, so risks of reviewer error and bias could not be ruled out. Use of a narrative synthesis appeared appropriate given the clinical heterogeneity of the included studies.

Uncertainty regarding the review process, a lack of formal quality assessment and clinical heterogeneity of the included studies mean that the conclusions should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors stated that physicians should note that antipsychotic agents were useful for treatment of stimulant-induced psychotic disorders, but should be cautious when using them at high doses for the long-term treatment of substance use disorders in stimulant users.

Research: The authors stated that further long-term large-scale studies were required to assess the effectiveness of clozapine on alcohol and cannabis dependence in comorbid psychosis patients. Large randomised trials were needed to determine the precise impact of atypical antipsychotic agents on stimulant dependence in comorbid psychosis patients. Studies were needed to investigate which groups of patients without comorbid conditions may benefit most from antipsychotics.

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