

COCHRANE CORNER

Pharmacological treatment for psychotic depression

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[†]This review is an abridged version of a Cochrane review previously published in the Cochrane Database of Systematic Reviews, 2015, Jul 23, Issue 7: CD004044 (see www.cochranelibrary.com for information). Cochrane reviews are regularly updated as new evidence emerges and in response to feedback, and the Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review.

We thank the Cochrane Review Group for their support in publishing these reviews.

See commentary on pp. 3–8, this issue.

Background

Evidence is limited regarding the most effective pharmacological treatment for psychotic depression: combination of an antidepressant plus an antipsychotic, monotherapy with an antidepressant or monotherapy with an antipsychotic. This is an update of a review first published in 2005 and last updated in 2009.

Objectives

1. To compare the clinical efficacy of pharmacological treatments for patients with an acute psychotic depression: antidepressant monotherapy, antipsychotic monotherapy and the combination of an antidepressant plus an antipsychotic, compared with each other and/or with placebo. 2. To assess whether differences in response to treatment in the current episode are related to non-response to prior treatment.

Search methods

A search of the Cochrane Central Register of Controlled Trials and the Cochrane Depression, Anxiety and Neurosis Group Register (CCDANCTR) was carried out (to 12 April 2013). These registers include reports of randomised controlled trials from the following bibliographic databases: EMBASE (1970–), MEDLINE (1950–) and PsycINFO (1960–). Reference lists of all studies and related reviews were screened and key authors contacted.

Selection criteria

All randomised controlled trials (RCTs) that included participants with acute major depression with psychotic features, as well as RCTs consisting of participants with acute major depression with or without psychotic features, that reported separately on the subgroup of participants with psychotic features.

Data collection and analysis

Two review authors independently extracted data and assessed risk of bias in the included studies, according to the criteria of the *Cochrane Handbook for Systematic Reviews of Interventions*.

Data were entered into RevMan 5.1. We used intention-to-treat data. For dichotomous efficacy outcomes, the risk ratio (RR) with 95% confidence intervals (CIs) was calculated. For continuously distributed outcomes, it was not possible to extract data from the RCTs. Regarding the primary outcome of harm, only overall drop-out rates were available for all studies.

Main results

The search identified 3659 abstracts, but only 12 RCTs with a total of 929 participants could be included in the review. Because of clinical heterogeneity, few meta-analyses were possible. The main outcome was reduction of severity (response) of depression, not of psychosis. We found no evidence for the efficacy of monotherapy with an antidepressant or an antipsychotic. However, evidence suggests that the combination of an antidepressant plus an antipsychotic is more effective than antidepressant monotherapy (three RCTs; RR 1.49, 95% CI 1.12–1.98, $P = 0.006$), more effective than antipsychotic monotherapy (four RCTs; RR 1.83, 95% CI 1.40–2.38, $P = 0.00001$) and more effective than placebo (two identical RCTs; RR 1.86, 95% CI 1.23–2.82, $P = 0.003$). Risk of bias is considerable: there were differences between studies with regard to diagnosis, uncertainties concerning randomisation and allocation concealment, differences in treatment interventions (pharmacological differences between the various antidepressants and antipsychotics) and different outcome criteria.

Authors' conclusions

Psychotic depression is very understudied, limiting confidence in the conclusions drawn. Some evidence indicates that combination therapy with an antidepressant plus an antipsychotic is more effective than either treatment alone or placebo. Evidence is limited for treatment with an antidepressant alone or with an antipsychotic alone.

Assessed as up to date: 12 April 2013