# ABSTRACTS OF COCHRANE SYSTEMATIC REVIEWS

In Cochrane corner this time again three systematic reviews have been selected. First is about the effectiveness of antipsychotics in psychotic depression, which has always remained debatable in clinical practice. In second review long and short term advantages of combined therapy have been evaluated in management of panic disorder. The third review is to assess the efficacy and tolerability of medication in adolescent and pediatric anxiety disorders.

1. Depression with psychotic symptoms is not an uncommon finding in clinical practice. However uncertainty prevails about the role of antipsychotics in this psychiatric disorder.

   In this review effectiveness of antipsychotics alone, or in combination with antidepressants have been assessed. Ten randomized control trials (RCTs) with 548 patients could satisfy the inclusion criteria. According to authors conclusion treatment with antipsychotic alone was never found effective. However starting with antidepressants and then adding antipsychotic if the patient shows inadequate response was declared as an appropriate option for the patients with psychotic depression.

2. As we know that panic disorder with or without agoraphobia is a sever anxiety disorders leading to significant impairment in important areas of functioning. Moreover long term effectiveness of routine interventional strategies has not been established and relapses are more common.

   In this review combined therapy i-e psychotherapy and antidepressants have been compared with either monotherapy alone. Twenty one randomized control trials (RCTs) involving behavior therapy or cognitive behavior therapy were evaluated At the end of acute phase treatment, combined therapy was found superior to antidepressant therapy alone. Moreover after the acute phase treatment psychotherapy alone was as effective as combined therapy. So there is a need to develop multidimensional approach towards management of anxiety disorders in developing countries.

3. Anxiety disorders are more common and potentially disabling in children and adolescent population. Early recognition and effectiveness of pharmacological and psychological interventions can be of much help in preventing long term disability. This systematic revieve of randomized control trials (RCTs) has evaluated the efficacy and tolerability of medication in pediatric anxiety disorders.

   Twenty two short term RCTs with reasonable sample size were found eligible for eligible for inclusion. Majority of trails were related to Obsessive compulsive disorder. According to the results though medication was less tolerated than placebo( as shown by significant drop out rate), but it was more effective in reducing overall symptom severity even across all anxiety disorders. Selective serotonin reuptake inhibitors were the main antidepressants tried in this review.

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## PHARMACOLOGICAL TREATMENT FOR PSYCHOTIC DEPRESSION

**Wijkstra J, Lijmer J, Balk F, Geddes J, Nolen WA**

### ABSTRACT

**Background:** Regarding the pharmacological treatment of psychotic depression there is uncertainty about the effectiveness of an antidepressant alone compared to the combination of an antidepressant and an antipsychotic.

**Objectives:** To compare the clinical effectiveness of pharmacological treatments for patients with a psychotic depression: antidepressant monotherapy, antipsychotic monotherapy, and the combination of an antidepressant and an antipsychotic, compared with each other and/or with placebo.

***Search strategy:***

(1) The Cochrane Central Register of Controlled Trials (CENTRAL) was screened with the terms depressive disorder and drug treatment (April 2004).

(2) MEDLINE (1966 to April 2004) and EMBASE (1980 to April 2004) were searched using terms with regard to treatment of unipolar psychotic depression.

(3) Reference lists of related reviews and reference lists of all identified studies were searched.

(4) Personal communications.

**Selection criteria**

All randomised controlled trials (RCTs) with patients with major depression with psychotic features as well as RCTs with patients with major depression with or without psychotic features which reported on the subgroup of patients with psychotic features separately.

***Data collection and analysis***

Two reviewers assessed the methodological quality of the included studies, according to the Cochrane Handbook criteria. Data were entered into RevMan 4.2.5. We used intention-to-treat data. For dichotomous efficacy outcomes, the relative risk with 95% confidence intervals (CI) was calculated. For continuously distributed outcomes, it was not possible to extract data from the RCTs. Regarding the primary harm outcome, only overall drop-out rates were available for all studies.

***Main results***

The search identified 3333 abstracts, but only 10 RCTs with a total of 548 patients could be included in the review. Due to clinical heterogeneity, few meta-analyses were possible. We found no conclusive evidence that the combination of an antidepressant and an antipsychotic is more effective than an antidepressant alone (two RCTs; RR 1.44, 95% CI 0.86 to 2.41), but a combination is more effective than an antipsychotic alone (three RCTs; RR 1.92, 95% CI 1.32 to 2.80). There were no statistically significant differences in the overall drop-out rates between any of the treatments, neither in individual studies nor after pooling of studies.

**Authors' conclusions**

Treatment with an antipsychotic alone is not a good option. Starting with an antidepressant alone and adding an antipsychotic if the patient does not respond or starting with the combination of an antidepressant and an antipsychotic both appear appropriate options for patients with psychotic depression. In clinical practice the balance between risks and benefits suggests that initial antidepressive monotherapy and adding an antipsychotic if there is inadequate response should be the preferred treatment strategy for many patients. The general lack of available data limits confidence in the conclusions drawn.

# COMBINED PSYCHOTHERAPY PLUS ANTIDEPRESSANTS FOR PANIC DISORDER WITH OR WITHOUT AGORAPHOBIA

**Furukawa TA, Watanabe N, Churchill R**

## ABSTRACT

**Background:** Panic disorder can be treated with pharmacotherapy, psychotherapy or in combination, but the relative merits of combined therapy have not been well established.

**Objectives:** To review evidence concerning short- and long-term advantages and disadvantages of combined psychotherapy plus antidepressant treatment for panic disorder with or without agoraphobia, in comparison with either therapy alone.

**Search strategy:** The Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Registers (CCDANCTR-Studies and CCDANCTR-References) were searched on 11/10/2005, together with a complementary search of the Cochrane Central Register of Controlled Trials and MEDLINE, using the keywords antidepressant and panic. A reference search, SciSearch and personal contact with experts were carried out.

***Selection criteria***

Two independent review authors identified randomised controlled trials comparing the combined therapy against either of the monotherapies among adult patients with panic disorder with or without agoraphobia.

***Data collection and analysis***

Two independent review authors extracted data using predefined data formats, including study quality indicators. The primary outcome was relative risk (RR) of "response" i.e. substantial overall improvement from baseline as defined by the original investigators. Secondary outcomes included standardised weighted mean differences in global severity, panic attack frequency, phobic avoidance, general anxiety, depression and social functioning and relative risks of overall dropouts and dropouts due to side effects.

***Main results***

We identified 23 randomised comparisons (representing 21 trials, 1709 patients), 21 of which involved behaviour or cognitive-behaviour therapies. In the acute phase treatment, the combined therapy was superior to antidepressant pharmacotherapy (RR 1.24, 95% confidence interval (CI) 1.02 to 1.52) or psychotherapy (RR 1.17, 95% CI 1.05 to 1.31). The combined therapy produced more dropouts due to side effects than psychotherapy (number needed to harm (NNH) around 26). After the acute phase treatment, as long as the drug was continued, the superiority of the combination over either monotherapy appeared to persist. After termination of the acute phase and continuation treatment, the combined therapy was more effective than pharmacotherapy alone (RR 1.61, 95% CI 1.23 to 2.11) and was as effective as psychotherapy (RR 0.96, 95% CI 0.79 to 1.16).

***Authors' conclusions***

Either combined therapy or psychotherapy alone may be chosen as first line treatment for panic disorder with or without agoraphobia, depending on patient preference.

# PHARMACOTHERAPY FOR ANXIETY DISORDERS IN CHILDREN AND ADOLESCENTS

**Ipser JC, Stein DJ, Hawkridge S, Hoppe L**

## ABSTRACT

**Background:** Anxiety disorders are a potentially disabling group of disorders which are prevalent in childhood and adolescence. The recognition of the early onset of anxiety disorders, and their successful treatment with medication in adults, has led to the growing interest in using medication for paediatric anxiety disorders.

**Objectives:** To assess the efficacy and tolerability of medication for treating paediatric anxiety disorders.

**Search strategy:** We searched the Cochrane Depression, Anxiety and Neurosis Group specialised register (CCDANCTR-Studies), MEDLINE (via PubMed 1966 to August 2008), EMBASE (1966 to August 2008), and PsycINFO (1972 to August 2008). Various electronic registers were searched for unpublished studies. Reference lists of retrieved articles were searched for additional studies.

***Selection criteria***

All randomised controlled trials (RCTs) of pharmacotherapy in childhood/adolescent anxiety disorders.

***Data collection and analysis***

Two raters independently assessed RCTs for inclusion in the review, collated trial data, and assessed trial quality. Investigators were contacted to obtain missing data. Summary statistics were stratified by medication class, and by medication agent for the selective serotonin reuptake inhibitors (SSRIs). Dichotomous and continuous measures were calculated using a random effects model, heterogeneity was assessed, and subgroup/sensitivity analyses were undertaken.

***Main results***

22 short-term (<= 16 weeks) RCTs were included in the analysis (2519 participants). The majority of the trials assessed the efficacy of the SSRIs (N = 15).

Medication and placebo response occurred in 58.1% and 31.5% of patients, respectively (Number of studies (N) = 14, Number needed to treat (NNT) = 4). Medication was more effective than placebo in reducing overall symptom severity in OCD in a post-hoc comparison (N = 7, Weighted Mean Difference (WMD) = -4.45, 95%CI = -5.94, -2.97, n = 765). Medication was less well tolerated than placebo overall, though the absolute proportion of participants who withdrew due to drug-related adverse events was low (4.9%).

***Authors' conclusions***

Medication treatments can be effective in paediatric anxiety disorders, acting to reduce core symptoms, and should be considered as part of the treatment of these disorders. The greatest number of trials showing efficacy to date have assessed the SSRIs in treating paediatric OCD.

There is no clear evidence to show that any particular class of medication is more effective or better tolerated than any other. As quantitative data was only available for the SSRIs and venlafaxine the routine use of benzodiazepines cannot be recommended, especially given concerns of dependency and treatment-related emergent adverse events associated with this class of drugs.

Future RCTs could help identify potential clinical moderators of treatment efficacy. Studies of the long-term efficacy of medication treatment, optimal dosage, as well as direct comparisons of pharmacotherapy and psychotherapy are also warranted.