ABSTRACTS OF COCHRANE SYSTEMATIC REVIEWS

Chochrane corner has this time focused on the role of antidepressants in psychiatric disorders other than the depressive disorders, such as schizophrenia and Generalized Anxiety Disorder. In another review evidence for the psychotic symptoms in epilepsy has been evaluated.

1 Generalized anxiety disorder (GAD) is not an uncommon psychiatric condition in primary and tertiary care settings. Uptil now there is routine practice of the use rather misuse of anxiolytics to treat this disabling disorder, leading to problem of tolerance and dependence. For the last few decades there is growing evidence for the effectiveness of antidepressants in the treatment of GAD. In this review fifteen clinical trials were included but only eight of them used recognized methods of diagnosis. Moreover only one study included adolescents in its population. However encouraging results were found regarding efficacy of antidepressants in GAD. Further trials are needed to confirm the evidence and also to compare the efficacy against benzodiazepine anxiolytics.

2 As we know that negative symptoms in schizophrenia have been a great challenge to psychiatrists in clinical practice. Atypical antipsychotics have helped to some extent but the problem has still been partially solved. Different add on strategies have been frequently introduced to address this issue and the use of antidepressants is one of them. In this review the outcome of combination of antidepressants with antipsychotics in case of negative symptoms of schizophrenia has been evaluated. Only five studies were included in the review. According to the results participants treated in "combination" showed statistically significant improvement as compared to control group. While for movement disorder and other adverse effects, no significant difference was found in any of the study. However the amount of information currently available is still limited and large well designed studies are justified to reach to the firm conclusion.

3. We know that experience of psychotic symptoms in epilepsy is a common occurrence. Moreover management of epilepsy combined with psychosis really poses a great challenge to clinicians because of compliance issues and adverse effects of antipsychotics on underlying neurological disorder. The authors have tried to evaluate the effectiveness of different intervention strategies in psychotic symptoms in epileptic patients. Surprisingly the authors could find only one study that could fulfill the inclusion criteria in this regard out of 492 studies reviewed. Results of few other studies could be of help in providing further information on this important management issue. Though "only one selected RCT" has proven the efficacy of antipsychotics in controlling psychotic symptoms but no mention has been made of typical and atypical antipsychotics or their effect on seizure control. However an important management issue has been highlighted in this review and further replications are needed in view of the present insufficient evidence.

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1. ANTIDEPRESSANTS FOR GENERALIZED ANXIETY DISORDER

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ABSTRACT

Background: Pharmacological treatments have been successfully used to treat Generalized Anxiety Disorder (GAD). Benzodiazepine and non benzodiazepine anxiolytics used to be the mainstay for the pharmacological treatment of GAD. However, data emerging over the last two decades have shown that antidepressants may be as effective as anxiolytics in this condition. The use of antidepressants may also be beneficial, because GAD often coexists with major depressive disorder (62% comorbidity) and dysthymia (37%).

Objectives: To assess the efficacy and acceptability of antidepressants for treating generalized anxiety disorder.

Search strategy: Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register - CCDANCTR (up to May 2002), Anxiety Neurosis (up to May 2002) and Cochrane Controlled Trials Register (CENTRAL/CCTR) (up to May 2002), MEDLINE (1966 to May 2002), LILACS (1982 to May 2002); reference searching; personal communication; conference abstracts and book chapters on the treatment of generalized anxiety disorder.

Selection criteria

Randomized controlled trials were included. Non randomized studies and those that included patients with both GAD and another Axis I co-morbidity were excluded.

Data collection and analysis

The data from studies were extracted independently by two reviewers. Relative risks, weighted mean difference and number needed to treat were estimated. People who died or dropped out were regarded as having had no improvement.

Main results

Antidepressants (imipramine, venlafaxine and paroxetine) were found to be superior to placebo in treating GAD. The calculated NNT for antidepressants in GAD is 5.15. Dropout rates did not differ between antidepressants. Only one study presented data on imipramine and trazodone. Imipramine was chosen as the reference drug and, therefore, data on trazodone could not be included in the meta analysis. Only one study was conducted among children and adolescents (Rynn 2000). This showed very promising results of sertraline in children and adolescents with GAD, which warrants replication in larger samples.

Authors' conclusions

The available evidence suggests that antidepressants are superior to placebo in treating GAD. There is evidence from one trial suggesting that paroxetine and imipramine have a similar efficacy and tolerability. There is also evidence from placebo-controlled trials suggesting that these drugs are well tolerated by GAD patients. Further trials of antidepressants for GAD will help to demonstrate which antidepressants should be used for which patients.

2. ANTIDEPRESSANTS FOR THE NEGATIVE SYMPTOMS OF SCHIZOPHRENIA

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ABSTRACT

Background: Negative symptoms are common in people with schizophrenia and are often difficult to treat with antipsychotic drugs. Treatment often involves the use of various add-on medications such as antidepressants.

Objectives: To review the effects of the combination of antipsychotic and antidepressant drug treatment for management of negative symptoms in schizophrenia and schizophrenia-like psychoses.

Search strategy: We searched the Cochrane Schizophrenia Group's register (January 2004). We also contacted authors of included studies in order to identify further trials.

Selection criteria

We included all randomized controlled trials comparing antipsychotic and antidepressant combinations with antipsychotics alone for the treatment of prominent negative symptoms in schizophrenia and/or schizophrenia-like psychoses.

Data collection and analysis

Working independently, we selected and critically appraised studies, extracted data and analyzed on an intention-to-treat basis. Where possible and appropriate we calculated the relative risk RR) and their 95% confidence intervals (CI), with the number needed to treat (NNT).

Main results

We included five studies (all short-term, total N=190). We found no significant difference for 'leaving the study early for any reason' between the antipsychotic plus antidepressant combination and the control group (n=90, 3 RCTs, RR 3.0 CI 0.35 to 26.04). Leaving early due to adverse events (n=64, 2 RCTs, RR 5.0 CI 0.26 to 97.0) and leaving the study early due to inefficacy (n=34, 1 RCT, RR 3.0 CI 0.13 to 68.84) also showed no significant difference between the two treatment groups. In terms of clinical response, participants treated with the antipsychotic plus antidepressant medications showed a statistically significant greater improvement (n=30, 1 RCT, WMD -1.0 CI -1.61 to -0.39) and showed a significantly lower severity at endpoint (n=30, 1 RCT, WMD -0.9 CI -1.55 to -0.25) on the Clinical Global Impression Scale than those treated with antipsychotics alone. More people allocated to combination therapy had a clinically significant improvement in negative symptoms compared with those given antipsychotics and placebo (n=60, 2 RCTs, RR 0.56 CI 0.32 to 0.97, NNT 3 CI 3 to 34). Significant differences in favour of the combination therapy were seen in different aspects of negative symptoms: 'affective flattening' (n=30, 1 RCT, WMD -7.0 CI -10.37 to -3.63), 'alogia' (n=26, 1 RCT, WMD -3.00 CI -5.14 to -0.86) and 'avolition' (n=30, 1 RCT, WMD -3.0 CI -5.04 to -0.96). No statistically significant difference was found between treatment groups in regards to the outcome 'at least one adverse event' (n=84, 2 RCTs, RR 1.80 CI 0.66 to 4.90). For movement disorders and other adverse effects, no statistically significant differences were found in any of the studies that provided usable data on these outcomes. There are no data at all

on outcomes such as compliance, cost, social and cognitive functioning, relapse, recurrence of negative symptoms, rehospitalisation or quality of life. There are no medium or long term data.

Authors' conclusions

The combination of antipsychotics and antidepressants may be effective in treating negative symptoms of schizophrenia, but the amount of information is currently too limited to allow any firm conclusions. Large, pragmatic, well-designed and reported long term trials are justified.

3. INTERVENTIONS FOR PSYCHOTIC SYMPTOMS CONCOMITANT WITH EPILEPSY

Farooq S, Sherin A

ABSTRACT

Background: People suffering from epilepsy have an increased risk of suffering from psychotic symptoms. The psychotic syndromes associated with epilepsy have generally been classified as ictal, postictal and interictal psychosis. Anticonvulsant drugs have been reported to precipitate psychosis. Moreover, all antipsychotic drugs have the propensity to cause paroxysmal EEG abnormalities and induce seizures.

Objectives: To evaluate the benefits of interventions used to treat clinically significant psychotic symptoms occurring in people with epilepsy with regard to global improvement, changes in mental state, hospitalization, behavior, quality of life, effect on the frequency of seizures and interaction with antiepileptic drugs.

Search strategy: We searched the Trials Registers of the Cochrane Schizophrenia Group and the Cochrane Epilepsy Group (May 2008), the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* Issue 2, 2008), MEDLINE (Ovid, 1950 to14 May 2008), EMBASE (1980 to 2006), PsycINFO (1872 to 12 May 2008), CINAHL (1981 to 9 May 2008) and Biological Abstracts using the Cochrane Schizophrenia Group's phrase for randomized controlled trials and schizophrenia or psychotic disorders combined with the phrase [and {epilepsy* or seizure disorders* }].

Two review authors (SF and AS) independently inspected the citations identified from the search. We identified potentially relevant abstracts and assessed full papers for inclusion and methodological quality.

Selection criteria

All randomized controlled trials comparing drugs, behavior therapy, cognitive behavior therapy or other non-pharmacological interventions used to relieve psychotic symptoms in people with epilepsy.

Data collection and analysis

We planned to extract and analyze the data from all relevant studies using standardized methods. As only one study met the inclusion criteria, no meta-analysis was attempted.

Main results

After independently assessing the abstracts and titles of 492 articles, we selected five relevant abstracts. Ultimately we found only one study meeting the inclusion criteria, which was available only as an abstract. This study compared the use of olanzapine (10 mg/day) with haloperidol (12 mg/day) in 16 patients suffering from schizophrenia-like psychosis of epilepsy (SLPE). Thirteen patients completed the study. Significant improvement was associated with use of olanzapine. We did not identify any study on psychosocial interventions in patients suffering from epilepsy and psychosis.

Authors' conclusions

Only one randomized controlled trial was found which lacked the power to test the efficacy of antipsychotics in those suffering from psychosis concomitant with epilepsy.

Limited evidence from this small RCT suggests an improvement in psychotic symptoms, but not other outcome measures, with the use of an antipsychotic. The effects on seizure control are not well studied. Further trials are required to inform practice.