

## ABSTRACTS OF COCHRANE SYSTEMATIC REVIEWS

In Cochrane corner we have again selected three important systematic reviews. First one is designed to evaluate the efficacy of Olanzapine in prophylaxis of Bipolar Affective Disorder and the other two are related to psychological interventions in the management of schizophrenia and post traumatic stress disorder, respectively. All these relate to the clinical problems we face in common practice, particularly the last review in view of current situation in Pakistan.

1. We know that Bipolar Affective Disorder (BAD) is a severe and common psychiatric disorder characterized by its recurrent nature. It emphasizes for the importance of effective long term intervention strategies to prevent relapse and decrease social and functional disability. Until recently, mood stabilizers were the mainstay of the prophylaxis but clinical studies show at best partial efficacy of these drugs. In this review an antipsychotic, Olanzapine has been evaluated in the long term management of BAD. Though only five studies could fulfil the inclusion criteria but the total sample size (1165 participants) was quiet reasonable. No statistically significant difference was found between Olanzapine and other mood stabilizers in preventing symptomatic relapse for any mood episode. However, Olanzapine was found more effective in preventing manic relapse as compared to Lithium. This has major implications. Lithium is difficult drug to manage , especially in developing country settings where the optimum conditions for monitoring lithium therapy may not always be present. However, it is important to remember that the depressive episodes in Bipolar Affaective Disorder last longer and are more disabling and this poses major challenge for any mood stabilizer.
2. Prognosis in schizophrenia has rightly been a major concern for clinicians. Poor prognosis in schizophrenic patients, besides many other factors, is usually attributed to inadequate drug adherence. As a result, compliance therapy is a major focus of attention among mental health professionals working in the field of schizophrenia. In this review, effect of compliance therapy has been assessed on antipsychotic medication adherence. It appears that authors have used fairly strict criteria for selecting studies as there are many studies which address the interventions to improve the drug adherence. (For a comprehensive systematic review please see, Zygmunt A, Olfson M, Boyer CA, Mechanic D. The interventions to improve medication adherence in schizophrenia. Am J

Psychiatry 2002;159:1653-64. This review presents a different coclusion). Only one study (n=56) qualified the inclusion criteria, showing no significant difference between compliance therapy and non specific counseling on primary outcome measure. However results of a single study with such a small sample size cannot be generalized and further studies with different designs are proposed to evaluate the effectiveness of this important psychological intervention in the management of schizophrenia.

- 3 In view of widespread terrorist activities in Pakistan, prevention of long term psychological distress following traumatic events is a major challenge for mental health professionals. In the past, single session psychological debriefing has been widely tried, but with poor outcome. In this review, effect of multiple session early psychological intervention has been examined in eleven studies with 941 participants. Again, there was no significant difference between treatment and control group to prevent the future psychological events. Alarmingly, there was some evidence for worse outcome in intervention group. This highlights the need to apply only evidence based intervention at the time of disaster as useful resources are often wasted during the initial phase of trauma on the intervention which may not work or perhaps make condition worse. This review presents major challenge for health professionals who arrive soon after disaster or trauma and provide counseling during the early phase.

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### 1. OLANZAPINE, IN LONG-TERM TREATMENT FOR BIPOLAR DISORDER

**Andrea Cipriani, Jennifer M Rendell,  
John Geddes**

#### ABSTRACT

**Background:** Many patients with bipolar disorder require long-term treatment to prevent recurrence. Antipsychotic drugs are often used to treat acute manic episodes. It is important to clarify whether olanzapine could

have a role in long-term prevention of manic and depressive relapses.

**Objectives:** To assess the effects of olanzapine, as monotherapy or adjunctive treatment, in preventing manic, depressive and mixed episodes in patients with bipolar affective disorder.

**Search strategy:** We searched the Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register (September 2006), the Cochrane Central Register of Controlled Trials (September 2006), MEDLINE (1966-December 2007), EMBASE (1980-2006), CINAHL (1982-2006), PsycINFO (1872-2006) and reference lists. We also contacted experts, trialists and pharmaceutical companies in the field.

### **Selection criteria**

Randomised controlled trials comparing olanzapine with placebo or other active treatment in long-term treatment of bipolar disorder.

### **Data collection and analysis**

Two review authors independently assessed trial quality and extracted data. We contacted study authors for additional information.

### **Main results**

Five trials (1165 participants) were included in the review. There was no statistically significant difference between olanzapine and placebo (either alone or in combination with lithium or valproate) in terms of number of participants who experienced relapse into mood episode (random effects RR 0.68, 95% CI 0.43 to 1.07,  $p = 0.09$ ; 2 studies,  $n=460$ ), however restricting the analysis to the trial that compared olanzapine monotherapy versus placebo, there was a statistically significant difference in favour of olanzapine (RR 0.58, 95% CI 0.49 to 0.69,  $p<0.00001$ ). No statistically significant difference was found between olanzapine and other mood stabilisers (lithium or valproate) in preventing symptomatic relapse for any mood episode, however, olanzapine was more effective than lithium in preventing symptomatic manic relapse (RR 0.59, 95% CI 0.39 to 0.89,  $p = 0.01$ ; 1 study,  $n=361$ ). Olanzapine either alone or as adjunctive treatment to mood stabilisers was associated with significantly greater weight gain than placebo. By contrast, olanzapine was associated with a lower rate of manic worsening, but with a higher rate of weight increase and depression than lithium.

### **Authors' conclusions**

Though based on a limited amount of information, there is evidence that olanzapine may prevent further mood episodes in patients who have responded to olanzapine during an index manic or mixed episode and who have not previously had a satisfactory response to lithium or valproate. However, notwithstanding these

positive results, the current evidence is stronger for lithium as first line maintenance treatment of bipolar disorder.

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## **COMPLIANCE THERAPY FOR SCHIZOPHRENIA**

**Andrew McIntosh, Louise Conlon, Stephen Lawrie, Andrew C Stanfield.**

### **ABSTRACT**

**Background:** Schizophrenia is a severe mental illness characterised by delusions and hallucinations. Antipsychotic drugs does reduce these symptoms, but at least half of people given these drugs do not comply with the treatment regimen prescribed.

**Objectives:** To assess the effects of compliance therapy on antipsychotic medication adherence for people with schizophrenia.

**Search strategy:** Cochrane Schizophrenia Group Trials Register (June 2005).

### **Selection criteria**

We included all randomised controlled trials of 'compliance therapy' for people with schizophrenia or related severe mental disorders.

### **Data collection and analysis**

We independently extracted data and, for dichotomous data, calculated the relative risk (RR), its 95% confidence interval (CI) on an intention to treat basis. We present continuous data using the weighted mean difference statistic.

### **Main results**

We included one trial with relevant and available data ( $n=56$ , duration 2 years) comparing compliance therapy with non-specific counseling. The primary outcome 'non-compliance with treatment' showed no significant difference between compliance therapy and non-specific counseling ( $n=56$ , RR 1.23 CI 0.74 to 2.05). The compliance therapy did not substantially effect attitudes to treatment ( $n=50$ , WMD DAI score -2.10 CI -6.11 to 1.91). Very few people ( $\sim 10\%$ ) left the study by one year ( $n=56$ , RR 0.5 CI 0.1 to 2.51). Mental state seemed unaffected by the therapy ( $n=50$ , WMD PANSS score 6.1 CI -4.54 to 16.74) as was insight ( $n=50$ , WMD SAI -0.5 CI -2.43 to 1.43), global functioning ( $n=50$ , WMD GAF -4.20 CI -16.42 to 8.02) and quality of life ( $n=50$ , WMD QLS -3.40 CI -16.25 to 9.45). At both one and two years the average number of days in hospital was non-significantly reduced for those allocated to the compliance therapy.

## **Authors' conclusions**

There is no clear evidence to suggest that compliance therapy is beneficial for people with schizophrenia and related syndromes but more randomized studies are justified and needed in order for this intervention to be fully examined.

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# **MULTIPLE SESSION EARLY PSYCHOLOGICAL INTERVENTIONS FOR THE PREVENTION OF POST-TRAUMATIC STRESS DISORDER**

**Neil P Roberts, Neil J Kitchiner,  
Justin Kenardy, Jonathan Bisson**

## **ABSTRACT**

**Background:** The prevention of long-term psychological distress following traumatic events is a major concern. Systematic reviews have suggested that individual Psychological Debriefing is not an effective intervention at preventing post traumatic stress disorder (PTSD). Recently other forms of intervention have been developed with the aim of preventing PTSD.

**Objectives** To examine the efficacy of multiple session early psychological interventions commenced within three months of a traumatic event aimed at preventing PTSD. Single session individual/group psychological interventions were excluded.

**Search strategy** Computerised databases were searched systematically, the most recent search was conducted in August 2008. The Journal of Traumatic Stress and the Journal of Consulting and Clinical Psychology were handsearched for the last two years. Personal communication was undertaken with key experts in the field.

## **Selection criteria**

Randomised controlled trials of any multiple session early psychological intervention or treatment (two or more sessions) designed to prevent symptoms of PTSD.

## **Data collection and analysis**

Data were entered using Review Manager software. The methodological quality of included studies was assessed individually by two review authors. Data were analysed for summary effects using Review Manager 4.2. Mean difference was used for meta-analysis of continuous outcomes and relative risk for dichotomous outcomes.

## **Main results**

Eleven studies with a total of 941 participants were found to have evaluated brief psychological interventions aimed at preventing PTSD in individuals exposed to a specific traumatic event, examining a heterogeneous range of interventions. Eight studies were entered into meta-analysis. There was no observable difference between treatment and control conditions on primary outcome measures for these interventions at initial outcome ( $k=5$ ,  $n=479$ ; RR 0.84; 95% CI 0.60 to 1.17). There was a trend for increased self-report of PTSD symptoms at 3 to 6 month follow-up in those who received an intervention ( $k=4$ ,  $n=292$ ; SMD 0.23; 95% CI 0.00 to 0.46). Two studies compared a memory structuring intervention against supportive listening. There was no evidence supporting the efficacy of this intervention.

## **Authors' conclusions**

The results suggest that no psychological intervention can be recommended for routine use following traumatic events and that multiple session interventions, like single session interventions, may have an adverse effect on some individuals. The clear practice implication of this is that, at present, multiple session interventions aimed at all individuals exposed to traumatic events should not be used. Further, better designed studies that explore new approaches to early intervention are now required.

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