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COCHRANE CORNER

ABSTRACTS OF COCHRANE SYSTEMATIC REVIEWS

In Cochrane Corner this time we highlight three issues which are subject of interesting systematic re- views. These, it is hoped will help to promote evidence based approach and identify the limited evidence we have about problems we face commonly.

1. Deliberate self harm (DSH) is defined as harming oneself intentionally, with or without suicidal intent. Pre- vious history of DSH is a strong predictor of future sui- cide, which is found in 40-60% of suicides. The WHO estimates that for every suicide, there are at least 10-20 DSH acts. Despite this the efficacy of psychosocial inter- vention in cases presenting with DSH remain is not well established. This also highlights an important advan- tage of the systematic reviews which help us to identify gaps in our knowledge. Systematic review by K Hawton et al. on Psychosocial and pharmacological treatments for deliberate self harm is an excellent endeavor.
2. History of psychiatry is replete with examples of initial enthusiasm followed by dismay. This is particu- larly true for drug treatment of schizophrenia. The dis- coveries of chlorpromazine in 1951 led to initial enthusi- asm and community care of patients with schizophre- nia. However this was followed by gruesome realization of irreversible side-effects like Tardive dyskinesia and Tardive dystonias. Atypical antipsychotics (AP) were received with similar fervor in the 90’s. Their side effects profile is different and undoubtedly better in some re- spects e.g extrapyramidal side effects and tardive dyskinesis... However, issues like metabolic syndrome, new onset Type-II diabetes mellitus surfaced as more and more longitudinal data become available.

Aripiprazole is one of the latest in series of atypi- cal antipsychotics.. This drug is claimed to have novel mechanism of action. Unlike dopamine receptor (D2) antagonism by conventional AP and D2 and 5-HT2 re- ceptor antagonism by atypical AP, Aripiprazole has a D2 agonist effect. The recent systematic review in Cochrane database of Systematic review by HG El-Sayeh and C Morganti helps to review the evidence related to this drug.

1. Depression has been described as a comorbid of various neuropsychiatric conditions. In stroke, depres- sion has been described in at least third to half of patients. There is ample literature to indicate that inci- dence of stroke is on the rise particularly among Asians. Pakistan is no exception to this trend. Rising pre- valence of hypertension is implicated as one of the major risk factors. The management of Post-stroke Depression (PSD) is complicated by the comorbid physi-

cal conditions, age group in which it commonly presents and neurological injury. However despite the high preva- lence of Post Stoke Depression (PSD) there is dearth of evidence on its prevention. The last systematic review presents some interesting findings in this regards.

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# PSYCHOSOCIAL AND PHARMACOLOGICAL TREATMENTS

FOR DELIBERATE SELF HARM

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K van Heeringen

## ABSTRACT

**Background:** Deliberate self-harm is a major health prob- lem associated with considerable risk of subsequent self-harm, including completed suicide.

**Objectives:** To identify and synthesise the findings from all randomised controlled trials that have examined the effectiveness of treatments of patients who have delib- erately harmed themselves.

**Search strategy:** Electronic databases screened: MEDLINE (from 1966-February 1999); PsycLit (from 1974-March 1999); Embase (from 1980-January 1999); The Cochrane Controlled Trials Register (CCTR) No.1 1999. Ten journals in the field of psychiatry and psychol- ogy were hand searched for the first version of this re- view. We have updated the hand search of three spe- cialist journals in the field of suicidal research until the end of 1998. Reference lists of papers were checked and trialists contacted.

### *Selection criteria*

All RCTs of psychosocial and/or psychopharma- cological treatment versus standard or less intensive types of aftercare for patients who shortly before enter- ing a study engaged in any type of deliberately initiated self-poisoning or self-injury, both of which are generally subsumed under the term deliberate self-harm.

### *Data collection and analysis*

Data were extracted from the original reports in- dependently by two reviewers. Studies were catego-

rized according to type of treatment. The outcome mea- sure used to assess the efficacy of treatment interven- tions for deliberate self-harm was the rate of repeated suicidal behaviour. We have been unable to examine other outcome measures as originally planned (e.g. com- pliance with treatment, depression, hopelessness, sui- cidal ideation/thoughts, change in problems/problem resolution).

### *Main results*

A total of 23 trials were identified in which repeti- tion of deliberate self-harm was reported as an outcome variable. The trials were classified into 11 categories. The summary odds ratio indicated a trend towards re- duced repetition of deliberate self-harm for problem-solv- ing therapy compared with standard aftercare (0.70; 0.45 to 1.11) and for provision of an emergency contact card in addition to standard care compared with standard aftercare alone (0.45; 0.19 to 1.07). The summary odds ratio for trials of intensive aftercare plus outreach com- pared with standard aftercare was 0.83 (0.61 to 1.14), and for antidepressant treatment compared with pla- cebo was 0.83 (0.47 to 1.48). The remainder of the com- parisons were in single small trials. Significantly reduced rates of further self-harm were observed for depot flupenthixol vs. placebo in multiple repeaters (0.09; 0.02 to 0.50), and for dialectical behaviour therapy vs. stan- dard aftercare (0.24; 0.06 to 0.93).

### *Authors’ conclusions*

There still remains considerable uncertainty about which forms of psychosocial and physical treatments of self-harm patients are most effective, inclusion of insuf- ficient numbers of patients in trials being the main limit- ing factor. There is a need for larger trials of treatments associated with trends towards reduced rates of repeti- tion of deliberate self-harm. The results of small single trials which have been associated with statistically sig- nificant reductions in repetition must be interpreted with caution and it is desirable that such trials are also repli- cated. *Cochrane Database of Systematic Reviews* 2006 Issue 4.

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# ARIPIPRAZOLE FOR SCHIZOPHRENIA

HG El-Sayeh and C Morganti

## ABSTRACT

**Background:** Treatment of people with schizophrenia using older typical antipsychotic drugs such as halo- peridol can be problematic. Many fail to respond to these older antipsychotics and more people experience dis- abling adverse effects. Aripiprazole is said to be one of

a new generation of atypical antipsychotics with good antipsychotic properties and minimal adverse effects.

**Objectives:** To evaluate the effects of aripiprazole for people with schizophrenia and schizophrenia-like psy- choses.

**Search strategy:** We searched the Cochrane Schizo- phrenia Group’s Register (September 2005) which is based on regular searches of BIOSIS, CENTRAL, CINAHL, EMBASE, MEDLINE and PsycINFO. We in-

spected references of all identified studies for further trials. We contacted relevant pharmaceutical companies, the FDA and authors of trials for additional information.

### *Selection criteria*

All clinical randomised trials comparing aripiprazole with placebo, typical or atypical antipsy- chotic drugs for schizophrenia and schizophrenia-like psychoses.

### *Data collection and analysis*

We extracted data independently. For homog- enous dichotomous data we calculated random effects, relative risk (RR), 95% confidence intervals (CI) and, where appropriate, numbers needed to treat (NNT) on an intention-to-treat basis. For continuous data, we cal- culated weighted mean differences (WMD).

### *Main results*

Despite the fact that 7110 people participated in fifteen randomised aripiprazole studies, we were un- able to extract any usable data on death, service out- comes, general functioning, behaviour, engagement with services, satisfaction with treatment; economic out- comes or cognitive functioning. Study attrition was very large and data reporting poor. Compared with placebo, aripiprazole significantly decreased relapse in both the short and medium term (n=300, 1 RCT, RR 0.66 CI 0.5 to 0.8, NNT 5 CI 4 to 8). It also produced better compliance with study protocol (n=2271, 8 RCTs, RR 0.72 CI 0.5 to 0.97, NNT 26 CI 16 to 239). Aripiprazole may decrease prolactin levels below that expected from placebo (n=305, 1 RCT, RR 0.32 CI 0.1 to 0.8, NNT 14 CI 11 to

50). Compared with typical antipsychotics there were no significant benefits for aripiprazole with regards to global state, mental state, quality of life or leaving the study early. Both groups reported similar rates of ad- verse effects, with the exception of akathisia (n= 955 RR

0.31 CI 0.2 to 0.6, NNT 20 CI 17 to 32) and the need for antiparkinson medication (n=1854, 4 RCTs, RR 0.45 CI

0.3 to 0.6, NNT 4 CI 3 to 5) which were lower in those receiving aripiprazole. When compared with olanzapine and risperidone, aripiprazole was no better or worse on outcomes of global state and leaving the study early. The rates of adverse effects were also similar, with the exception of less elevation of prolactin (n=301, 1 RCT, RR 0.04 CI 0.02 to 0.1, NNT 2 CI 1 to 2.5) and less prolongation of the average QTc (30 mg/day) (n=200, 1

RCT, WMD -10.0, CI -16.99 to -3.0) compared with risperidone. When compared with standard care (mixed group receiving typical and atypical antipsychotics) one aripiprazole study did have significantly less people not responding to treatment (n=1599, RR 0.70 CI 0.7 to 0.8, NNT 5 CI 4 to 6 ), not satisfied with care (n=1599, RR

0.62 CI 0.6 to 0.7, NNT 4 CI 4 to 5) and less people leaving the study early (n=1599, 1 RCT, RR 0.81 CI 0.7 to 0.9, NNT 13 CI 8 to 39). Results from the five new papers identified from the updated review search, did not significantly alter the main results or conclusions of the original review.

### *Authors’ conclusions*

Aripiprazole may be effective for the treatment of schizophrenia, but it does not differ greatly from typical and atypical antipsychotics with respect to treatment re- sponse, efficacy or tolerability. In comparison with typi- cal antipsychotics, aripiprazole may have a lower risk of akathisia, and in comparison to atypical antipsychotics, less risk of raised prolactin and prolongation of the QTc interval. Clearly reported pragmatic short, medium and long term randomised controlled trials should be un- dertaken to determine its position in everyday clinical practice.

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# INTERVENTIONS FOR

PREVENTING DEPRESSION AFTER STROKE

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## ABSTRACT

**Background: Abnormal mood is an important conse- quence of str**oke and may affect recovery and outcome. However, depression and anxiety are often not detected or inadequately treated. This may in part be due to doubts about whether anti-depressant treatments commenced early after the onset of stroke will prevent depression and improve outcome.

**Objectives:** To determine if pharmaceutical or psycho- logical interventions can prevent the onset of depres- sion, including depressive illness and abnormal mood, and improve physical and psychological outcomes, in patients with stroke.

**Search strategy:** We searched the Cochrane Stroke Group trials register (June 2003). In addition we searched the following electronic databases: Cochrane Central Register of Controlled Trials (*The Cochrane Li- brary,* Issue 3, 2002), MEDLINE (1966 to September

2002), EMBASE (1980 to September 2002), CINAHL

(1982 to September 2002), PsychINFO (1967 to Sep- tember 2002), Applied Science and Technology Plus (1986 to September 2002), Arts and Humanities Index (1991 to September 2002), Biological Abstracts (1969 to September 2002), General Science Plus (1994 to September 2002), Science Citation Index (1992 to Sep- tember 2002), Social Sciences Citation Index (1991 to September 2002), and Sociofile (1974 to September 2002). Reference lists from relevant articles and text- books were searched, and authors of known studies and pharmaceutical companies who manufacture psycho- tropic medications were contacted.

### *Selection criteria*

Randomised and quasi-randomised controlled tri- als comparing different types of pharmaceutical agents (eg selective serotonin reuptake inhibitors) with placebo, or various forms of psychotherapy against standard care (or attention control), in patients with a recent clinical diagnosis of stroke, where the treatment was undertaken with the explicit intention of preventing depression.

### *Data collection and analysis*

The primary analyses focussed on the proportion of patients who met the standard diagnostic criteria for depression applied in the trials at the end of follow-up. Secondary outcomes included depression or mood scores on standard scales, disability or physical func- tion, death, recurrent stroke, and adverse effects.

### *Main results*

Twelve trials involving 1245 participants were in- cluded in the review. Data were available for nine trials (11 comparisons) involving different pharmaceutical agents, and three trials of psychotherapy. The time from stroke onset to entry ranged from a few hours to six months, but most patients were recruited within one month of acute stroke. The duration of treatments ranged from two weeks to one year. There was no clear effect of pharmacological therapy on the prevention of depres- sion or on other measures. A significant improvement in mood was evident for psychotherapy, but this treatment effect was small and from a single trial. There was no effect on diagnosed depression.

### *Authors’ conclusions*

This review identified a small but significant effect of psychotherapy on improving mood, but no effect of either pharmacotherapy or psychotherapy on the pre- vention of depressive illness, disability, or other out- comes. More evidence is therefore required before any recommendations can be made about the routine use of such treatments to improve recovery after stroke.

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