ABSTRACTS OF COCHRANE SYSTEMATIC REVIEWS

In Cochrane Corner this time we highlight three issues which are subject of interesting systematic reviews. 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. Previous history of DSH is a strong predictor of future suicide, 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 intervention in cases presenting with DSH remain is not well established. This also highlights an important advantage 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 particularly true for drug treatment of schizophrenia. The discoveries of chlorpromazine in 1951 led to initial enthusiasm and community care of patients with schizophrenia. 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 respects 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 atypical antipsychotics.. This drug is claimed to have novel mechanism of action. Unlike dopamine receptor (D_2) antagonism by conventional AP and D_2 and 5-HT_2 receptor antagonism by atypical AP, Aripiprazole has a D_2 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.

3. Depression has been described as a comorbid of various neuropsychiatric conditions. In stroke, depression has been described in at least third to half of patients. There is ample literature to indicate that incidence of stroke is on the rise particularly among Asians. Pakistan is no exception to this trend. Rising prevalence of hypertension is implicated as one of the major risk factors. The management of Post-stroke Depression (PSD) is complicated by the comorbid physical conditions, age group in which it commonly presents and neurological injury. However despite the high prevalence 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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1. PSYCHOSOCIAL AND PHARMACOLOGICAL TREATMENTS FOR DELIBERATE SELF HARM

K Hawton, E Townsend, E Arensman, D Gunnell, P Hazell, A House, K van Heeringen

ABSTRACT

Background: Deliberate self-harm is a major health problem 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 deliberately 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 psychology were hand searched for the first version of this review. We have updated the hand search of three specialist 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 psychopharmacological treatment versus standard or less intensive types of aftercare for patients who shortly before entering 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 independently by two reviewers. Studies were catego-

rized according to type of treatment. The outcome measure used to assess the efficacy of treatment interventions 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. compliance with treatment, depression, hopelessness, suicidal ideation/thoughts, change in problems/problem resolution).

Main results

A total of 23 trials were identified in which repetition 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 reduced repetition of deliberate self-harm for problem-solving 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 compared with standard aftercare was 0.83 (0.61 to 1.14), and for antidepressant treatment compared with placebo was 0.83 (0.47 to 1.48). The remainder of the comparisons 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. standard 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 insufficient numbers of patients in trials being the main limiting factor. There is a need for larger trials of treatments associated with trends towards reduced rates of repetition of deliberate self-harm. The results of small single trials which have been associated with statistically significant reductions in repetition must be interpreted with caution and it is desirable that such trials are also replicated. *Cochrane Database of Systematic Reviews* 2006 Issue 4.

2. ARIPIPRAZOLE FOR SCHIZOPHRENIA

HG El-Sayeh and C Morganti

ABSTRACT

Background: Treatment of people with schizophrenia using older typical antipsychotic drugs such as haloperidol can be problematic. Many fail to respond to these older antipsychotics and more people experience disabling 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 psychoses.

Search strategy: We searched the Cochrane Schizophrenia Group's Register (September 2005) which is based on regular searches of BIOSIS, CENTRAL, CINAHL, EMBASE, MEDLINE and PsycINFO. We inspected 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 antipsychotic drugs for schizophrenia and schizophrenia-like psychoses.

Data collection and analysis

We extracted data independently. For homogenous 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 calculated weighted mean differences (WMD).

Main results

Despite the fact that 7110 people participated in fifteen randomised aripiprazole studies, we were unable to extract any usable data on death, service outcomes, general functioning, behaviour, engagement with services, satisfaction with treatment; economic outcomes 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 adverse 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 response, efficacy or tolerability. In comparison with typical 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 undertaken to determine its position in everyday clinical practice.

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3.INTERVENTIONS FOR PREVENTING DEPRESSION AFTER STROKE

CS Anderson, ML Hackett, AO House

ABSTRACT

Background: Abnormal mood is an important consequence of stroke 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 psychological interventions can prevent the onset of depression, 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 Library,* Issue 3, 2002), MEDLINE (1966 to September 2002), EMBASE (1980 to September 2002), CINAHL (1982 to September 2002), PsychINFO (1967 to September 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 September 2002), Social Sciences Citation Index (1991 to September 2002), and Sociofile (1974 to September 2002). Reference lists from relevant articles and textbooks were searched, and authors of known studies and pharmaceutical companies who manufacture psychotropic medications were contacted.

Selection criteria

Randomised and quasi-randomised controlled trials 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 function, death, recurrent stroke, and adverse effects.

Main results

Twelve trials involving 1245 participants were included 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 depression 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 prevention of depressive illness, disability, or other outcomes. 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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