BACKGROUND: Many people with schizophrenia do not achieve a satisfactory treatment response with ordinary antipsychotic drug treatment. In these cases, various add-on medications are used, among them benzodiazepines. OBJECTIVES: To review the effects of benzodiazepines for the treatment of schizophrenia and schizophrenia-like psychoses. SEARCH STRATEGY: The reviewers searched the Cochrane Schizophrenia Group’s register (last search March 2005). This register is compiled by methodical searches of BIOSIS, CINAHL, Dissertation abstracts, EMBASE, LILACS, MEDLINE, PSYNDEX, PsycINFO, RUSSMED, Sociofile, supplemented with hand searching of relevant journals and numerous conference proceedings. We also contacted authors of relevant studies in order to obtain missing data from existing trials. SELECTION CRITERIA: All randomised controlled trials comparing benzodiazepine to antipsychotics or to placebo (or no intervention), whether as sole treatment or as an adjunct to antipsychotic medication for the treatment of schizophrenia and/or schizophrenia-like psychoses. DATA COLLECTION AND ANALYSIS: We independently inspected abstracts, selected studies and re-inspected and quality assessed the full reports. We independently extracted relevant outcomes. Dichotomous data were analysed using relative risks (RR) and the 95% confidence intervals (CI). Continuous data were analysed using weighted mean differences. Where possible the number needed to treat...
(NNT) or number needed to harm (NNH) statistics were calculated. MAIN RESULTS: The review currently includes 31 studies with over 2000 participants. Most studies were small, of short duration - one to 13 weeks - and inconsistently and incompletely reported. Eight studies compared benzodiazepines as a sole agent with placebo. More participants receiving benzodiazepines showed a clinically significant response (n=222, 4 RCTs, RR 0.54 CI 0.3 to 1.0, NNT 3 CI 2 to 17). Only one small study found a significant group difference in favour of benzodiazepines regarding the improvement in overall BPRS mental state. Different rating scales were used to assess general mental state, and therefore many outcomes could not be pooled and no overall direction of effect emerged. Some adverse events observed in these studies suggested that benzodiazepines were more harmful than placebos but again the data were incompletely reported and without overall effect. Thirteen studies examined the effects of benzodiazepines in comparison to antipsychotics as a sole treatment. Trials that reported on clinical response found no advantage for any treatment group concerning improvement of the participants' global state, except of one small study that analysed the mean CGI severity score at one hour. This comparison is highly limited by the low numbers of studies reporting on global function and the short trial duration. Two studies showed a statistically significant superiority of antipsychotics in terms of relapse prevention at one year. Desired sedation occurred significantly more often among participants in the benzodiazepine group than among participants in the antipsychotic treatment group at 20 (n=301, 1 RCT, RR 1.32 CI 1.2 -1.5, NNT 5, CI 3 to 8) and 40 minutes(n= 301, 1 RCT, RR 1.13 CI 1.0 to 1.2, NNT 9 CI 6 to 33), but not at 30, 60 or 12 minutes. Other outcomes relating to the general or specific mental state revealed no significant differences between groups. As far as adverse events were reported there were no results in favour of any group. Sixteen studies examined whether the augmentation of antipsychotics with benzodiazepines is more effective than antipsychotics as a sole treatment. During the first hour of treatment the combination treatment group benefited from the additional benzodiazepine in terms of the participants global state. This benefit diminished over time and was not reproducible at 2 hours or longer. No superior efficacy of benzodiazepine augmentation could be found regarding the general mental state. Specific aspects of the mental state showed no group difference except for desired sedation at 30 and 60 minutes. Somnolence affected the combination treatment group significantly more than the control group (n=118, 2 RCTs, RR 3.30 CI 1.0 to 10.4, NNH 8 CI 5 to 50). We found use of antiparkinson medication to be less frequently used in the combination treatment group (n=282, RR 0.68 CI 0.5 to 1.0, NNH 9 CI 6 to 48). Adverse events were poorly reported and the results were based on very little data. AUTHORS' CONCLUSIONS: Randomised trial-derived evidence is currently too poor to recommend benzodiazepines neither as a sole nor as an adjunctive agent in schizophrenia or schizophrenia-like psychoses. The only significant effects were seen in terms of short-term sedation, at best. The evidence available on augmentation of antipsychotics with benzodiazepines is inconclusive and justifies large, simple and well-designed future trials focusing on clinical response, mental state, aggressive behaviour and adverse events.