Abstract:
In many countries of the industrialised world second generation ("atypical") antipsychotics have become the first line drug treatment for people with schizophrenia. The question as to whether, and if so how much, the effects of the various second generation antipsychotics differ is a matter of debate. In this review we examined how the efficacy and tolerability of olanzapine differs from that of other second generation antipsychotics. To evaluate the effects of olanzapine compared to other atypical antipsychotics for people with schizophrenia and schizophrenia-like psychosis.

1. Electronic searching
We searched the Cochrane Schizophrenia Group Trials Register (April 2007) which is based on regular searches of BIOSIS, CENTRAL, CINAHL, EMBASE, MEDLINE and PsycINFO.

2. Reference searching
We inspected the reference of all identified studies for more trials.

3. Personal contact
We contacted the first author of each included study for missing information.

4. Drug companies
We contacted the manufacturers of all atypical antipsychotics included for additional data. We included all randomised trials that used at least single-blind (rater-blind) design, comparing oral olanzapine with oral forms of amisulpride, aripiprazole, clozapine, quetiapine, risperidone, sertindole, ziprasidone or zotepine in people with schizophrenia or schizophrenia-like psychosis. We extracted data independently. For dichotomous data we calculated
relative risks (RR) and their 95% confidence intervals (CI) on an intention-to-treat basis based on a random effects model. We calculated numbers needed to treat/harm (NNT/NNH) where appropriate. For continuous data, we calculated weighted mean differences (WMD) again based on a random effects model. The review currently includes 50 studies and 9476 participants which provided data for six comparisons (olanzapine compared to amisulpride, aripiprazole, clozapine, quetiapine, risperidone or ziprasidone). The overall attrition from the included studies was considerable (49.2%) leaving the interpretation of results problematic. Olanzapine improved the general mental state (PANSS total score) more than aripiprazole (2 RCTs, n=794, WMD -4.96 CI -8.06 to -1.85), quetiapine (10 RCTs, n=1449, WMD -3.66 CI -5.39 to -1.93), risperidone (15 RCTs, n=2390, WMD -1.94 CI -3.31 to -0.58) and ziprasidone (4 RCTs, n=1291, WMD -8.32 CI -10.99 to -5.64), but not more than amisulpride or clozapine. This somewhat better efficacy was confirmed by fewer participants in the olanzapine groups leaving the studies early due to inefficacy of treatment compared to quetiapine (8 RCTs, n=1563, RR 0.56 CI 0.44 to 0.70, NNT 11 CI 6 to 50), risperidone (14 RCTs, n=2744, RR 0.78 CI 0.62 to 0.98, NNT 50 CI 17 to 100) and ziprasidone (5 RCTs, n=1937, RR 0.64 CI 0.51 to 0.79, NNT 17, CI 11 to 33). Fewer participants in the olanzapine group than in the quetiapine (2 RCTs, n=876, RR 0.56 CI 0.41 to 0.77, NNT 11 CI 7 to 25) and ziprasidone (2 RCTs, n=766, RR 0.65 CI 0.45 to 0.93, NNT 17 CI 9 to 100) treatment groups, but not in the clozapine group (1 RCT, n=980, RR 1.28 CI 1.02 to 1.61, NNH not estimable), had to be re-hospitalised in the trials. Except for clozapine, all comparators induced less weight gain than olanzapine (olanzapine compared to amisulpride: 3 RCTs, n=671, WMD 2.11kg CI 1.29kg to 2.94kg; aripiprazole: 1 RCT, n=90, WMD 5.60kg CI 2.15kg to 9.05kg; quetiapine: 7 RCTs, n=1173, WMD 2.68kg CI 1.10kg to 4.26kg; risperidone: 13 RCTs, n=2116, WMD 2.61kg CI 1.48kg to 3.74kg; ziprasidone: 5 RCTs, n=1659, WMD 3.82kg CI 2.96kg to 4.69kg). Associated problems such as glucose and cholesterol increase were usually also more frequent in the olanzapine group. Other differences in adverse effects were less well documented. Nevertheless, olanzapine may be associated with slightly more extrapyramidal side effects than quetiapine (use of antiparkinson medication (6 RCTs, n=1090, RR 2.05 CI 1.26 to 3.32, NNH 25 CI 14 to 100), but less than risperidone (use of antiparkinson medication 13 RCTs, n=2599, RR 0.78 CI 0.65 to 0.95, NNH 17 CI 9 to 100) and ziprasidone (use of antiparkinson medication 4 RCTs, n=1732, RR 0.70 CI 0.50 to 0.97, NNH not estimable). It may also increase prolactin somewhat more than aripiprazole, clozapine and quetiapine, but clearly less so than risperidone (6 RCTs, n=1291, WMD -22.84 CI -27.98 to -17.69). Olanzapine may be a somewhat more efficacious drug than some other second generation antipsychotic drugs. This small superiority in efficacy needs to be weighed against a larger weight gain and associated metabolic problems than most other second generation antipsychotic drugs, except clozapine. These conclusions are tentative due to the large number of people leaving the studies early which possibly limits the validity of the findings. Further large, well-designed trials are necessary to establish the relative effects of different second generation antipsychotic drugs.
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