Clozapine versus other atypical antipsychotics for schizophrenia.

Abstract:

Clozapine is an atypical antipsychotic demonstrated to be superior in the treatment of refractory schizophrenia which causes fewer movement disorders. Clozapine, however, entails a significant risk of serious blood disorders such as agranulocytosis which could be potentially fatal. Currently there are a number of newer antipsychotics which have been developed with the purpose to find both a better tolerability profile and a superior effectiveness. To compare the clinical effects of clozapine with other atypical antipsychotics (such as amisulpride, aripiprazole, olanzapine, quetiapine, risperidone, sertindole, ziprasidone and zotepine) in the treatment of schizophrenia and schizophrenia-like psychoses. We searched the Cochrane Schizophrenia Groups Register (June 2007) and reference lists of all included randomised controlled trials. We also manually searched appropriate journals and conference proceedings relating to clozapine combination strategies and contacted relevant pharmaceutical companies. All relevant randomised, at least single-blind trials, comparing clozapine with other atypical antipsychotics, any dose and oral formulations, for people with schizophrenia or related disorders. We selected trials and extracted data independently. For dichotomous data we calculated relative risks (RR) and their 95% confidence intervals (CI) based on a random-effects model. We calculated numbers needed to treat/harm (NNT/NNH) where
appropriate. For continuous data, we calculated mean differences (MD) again based on a random-effects model. The review currently includes 27 blinded randomised controlled trials, which involved 3099 participants. Twelve randomised control trials compared clozapine with olanzapine, five with quetiapine, nine with risperidone, one with ziprasidone and two with zotepine. Attrition from these studies was high (overall 30.1%), leaving the interpretation of results problematic. Clozapine had a higher attrition rate due to adverse effects than olanzapine (9 RCTs, n=1674, RR 1.60 CI 1.07 to 2.40, NNT 25 CI 15 to 73) and risperidone (6 RCTs, n=627, RR 1.88 CI 1.11 to 3.21, NNT 16 CI 9 to 59). Fewer participants in the clozapine groups left the trials early due to inefficacy than risperidone (6 RCTs, n=627, RR 0.40 CI 0.23 to 0.70, NNT 11 CI 7 to 21), suggesting a certain higher efficacy of clozapine. Clozapine was more efficacious than zotepine in improving the participants general mental state (BPRS total score: 1 RCT, n=59, MD -6.00 CI -9.83 to -2.17), but not consistently more than olanzapine, quetiapine, risperidone and ziprasidone. There was no significant difference between clozapine and olanzapine or risperidone in terms of positive or negative symptoms of schizophrenia. According to two studies from China quetiapine was more efficacious for negative symptoms than clozapine (2 RCTs, n=142, MD 2.32 CI 0.99 to 3.48). Clozapine produced somewhat fewer extrapyramidal side-effects than risperidone (use of antiparkinson medication: 6 RCTs, n=304, RR 0.39 CI 0.22 to 0.68, NNT 7 CI 5 to 18) and zotepine (n=59, RR 0.05 CI 0.00 to 0.86, NNT 3 CI 2 to 5). More participants in the clozapine group showed decreased white blood cells than those taking olanzapine, more hypersalivation and sedation than those on olanzapine, risperidone and quetiapine and more seizures than people on olanzapine and risperidone. Also clozapine produced an important weight gain not seen with risperidone. Other differences in adverse effects were less documented and should be replicated, for example, clozapine did not alter prolactin levels whereas olanzapine, risperidone and zotepine did; compared with quetiapine, clozapine produced a higher incidence of electrocardiogram (ECG) alterations; and compared with quetiapine and risperidone clozapine produced a higher increase of triglyceride levels. Other findings that should be replicated were: clozapine improved social functioning less than risperidone and fewer participants in the clozapine group had to be hospitalised to avoid suicide attempts compared to olanzapine. Other important outcomes such as service use, cognitive functioning, satisfaction with care or quality of life were rarely reported. Clozapine may be a little more efficacious than zotepine and risperidone but further trials are required to confirm this finding. Clozapine differs more clearly in adverse effects from other second generation antipsychotics and the side-effect profile could be key in the selection of treatment depending on the clinical situation and a patient's preferences. Data on other important outcomes such as cognitive functioning, quality of life, death or service use are currently largely missing, making further large and well-designed trials necessary. It is also important to take into account that the large number of people leaving the studies early limits the validity and interpretation of our findings.

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