Abstract:
Perphenazine is an old phenothiazine antipsychotic with a potency similar to haloperidol. It has been used for many years and is popular in the northern European countries and Japan. To examine the clinical effects and safety of perphenazine for those with schizophrenia and schizophrenia-like psychoses.

We updated our original search using the Cochrane Schizophrenia Group’s register (September 2013), references of all included studies and contacted pharmaceutical companies and authors of included studies in order to identify further trials.

We included all randomised controlled trials that compared perphenazine with other treatments for people with schizophrenia and/or schizophrenia-like psychoses. We excluded trials of depot formulations of perphenazine.

Two review authors independently inspected citations and, where possible, abstracts. We ordered papers, inspected and quality assessed them. We extracted data, again working independently. If loss to follow-up was greater than 50% we considered results as 'prone to bias'. For dichotomous data, we calculated risk ratios (RR) and for continuous data we calculated mean differences (MD), both with the 95% confidence intervals (CI).

We assessed quality of data using the GRADE (Grading of Recommendations Assessment, Development and Evaluation tool) and assessed risk of bias for included studies. Thirty-one studies fulfilled the inclusion criteria, with a total of 4662 participants (of which 4522 were receiving the drugs relevant to our
comparison) and presented data that could be used for at least one comparison. The trial centres were located in Europe (especially Scandinavia), Japan and Northern America. When comparing perphenazine with placebo, for our primary outcome of clinical response, results favoured perphenazine with significantly more people receiving placebo rated as either 'no better or deterioration' for global state than people receiving perphenazine (1 RCT, n = 61 RR 0.32 CI 0.13 to 0.78, very low quality evidence). More people receiving placebo relapsed, although not a statistically significant number (1 RCT, n = 48, RR 0.14 CI 0.02 to 1.07, very low quality evidence). Death was not reported in the perphenazine versus placebo comparison. Experiences of dystonia were equivocal between groups (1 RCT, n = 48, RR 1.00 CI 0.07 to 15.08, very low quality evidence); other outcomes not reported in this comparison include serious adverse events, economic outcomes, and service use and hospitalisation. For the comparison of perphenazine versus any other antipsychotic drugs, no real differences in effect between the drugs were found. There was no significant difference between groups for those considered 'no better or deterioration' (17 RCTs, n = 1879, RR 1.04 CI 0.91 to 1.17, very low quality evidence). For mental state outcome of 'no effect' of the study drug, there was again no significant difference between groups (4 RCTs, n = 383, RR 1.24 CI 0.61 to 2.52, very low quality evidence). Death was not reported in any of the included studies. There was no significant difference in rates of dystonia with perphenazine versus any other antipsychotic drugs (4 RCTs, n = 416, RR 1.36 CI 0.23 to 8.16, very low quality evidence), nor was there a significant difference between groups for serious adverse events (2 RCTs, n = 1760, RR 0.98 CI 0.68 to 1.41, very low quality evidence). Although perphenazine has been used in randomised trials for more than 50 years, incomplete reporting and the variety of comparators used made it impossible to draw clear conclusions. All data for the main outcomes in this review were of very low quality evidence. At best we can say that perphenazine showed similar effects and adverse events as several of the other antipsychotic drugs. Since perphenazine is a relatively inexpensive and frequently used compound, further trials are justified to clarify the properties of this classical antipsychotic drug.

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