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[Intervention Review]

Fluphenazine (oral) versus placebo for schizophrenia

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ABSTRACT

Background

Fluphenazine is one of the first drugs to be classed as an 'antipsychotic' and has been widely available for five decades.

Objectives

To compare the effects of oral fluphenazine with placebo for the treatment of schizophrenia. To evaluate any available economic studies and value outcome data.

Search methods

We searched the Cochrane Schizophrenia Group's Trials Register (23 July 2013, 23 December 2014, 9 November 2016 and 28 December 2017) which is based on regular searches of CINAHL, BIOSIS, AMED, EMBASE, PubMed, MEDLINE, PsycINFO, and registries of clinical trials. There is no language, date, document type, or publication status limitations for inclusion of records in the register.

Selection criteria

We sought all randomised controlled trials comparing oral fluphenazine with placebo relevant to people with schizophrenia. Primary outcomes of interest were global state and adverse effects.

Data collection and analysis

For the effects of interventions, a review team inspected citations and abstracts independently, ordered papers and re-inspected and quality assessed trials. We extracted data independently. Dichotomous data were analysed using fixed-effect risk ratio (RR) and the 95% confidence interval (CI). Continuous data were excluded if more than 50% of people were lost to follow-up, but, where possible, mean differences (MD) were calculated. Economic studies were searched and reliably selected by an economic review team to provide an economic summary of available data. Where no relevant economic studies were eligible for inclusion, the economic review team valued the already-included effectiveness outcome data to provide a rudimentary economic summary.

Main results

From over 1200 electronic records of 415 studies identified by our initial search and this updated search, we excluded 48 potentially relevant studies and included seven trials published between 1964 and 1999 that randomised 439 (mostly adult participants). No new included trials were identified for this review update. Compared with placebo, global state outcomes of 'not improved or worsened' were not significantly different in the medium term in one small study (n = 50, 1 RCT, RR 1.12 CI 0.79 to 1.58, *very low quality of evidence*). The risk of relapse in the long term was greater in two small studies in people receiving placebo (n = 86, 2 RCTs, RR 0.39 CI 0.05 to 3.31, *very low quality of evidence*), however with high degree of heterogeneity in the results. Only one person allocated fluphenazine was reported in the same small study to have died on long-term follow-up (n = 50, 1 RCT, RR 2.38 CI 0.10 to 55.72, *low quality of evidence*). Short-term extrapyramidal adverse effects were significantly more frequent with fluphenazine compared to placebo in two other studies for the outcomes of akathisia (n =



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227, 2 RCTs, RR 3.43 CI 1.23 to 9.56, moderate quality of evidence) and rigidity (n = 227, 2 RCTs, RR 3.54 CI 1.76 to 7.14, moderate quality of evidence). For economic outcomes, we valued outcomes for relapse and presented them in additional tables.

Authors' conclusions

The findings in this review confirm much that clinicians and recipients of care already know, but they provide quantification to support clinical impression. Fluphenazine's global position as an effective treatment for psychoses is not threatened by the outcome of this review. However, fluphenazine is an imperfect treatment and if accessible, other inexpensive drugs less associated with adverse effects may be an equally effective choice for people with schizophrenia.

PLAIN LANGUAGE SUMMARY

Fluphenazine versus Placebo for Schizophrenia

Review question: Is fluphenazine effective for the treatment of schizophrenia compared with placebo?

Background

Fluphenazine is one of the first drugs to be classed as an 'antipsychotic' and has been widely available for decades.

Searching for evidence

We updated the electronic search in December 2017 for trials that randomised people with schizophrenia to receive oral fluphenazine or placebo. No new studies were found to be added in this update.

Evidence found

Seven trials met the review requirements and provided useable data. The evidence currently available is of poor quality and suggests that whilst fluphenazine is a potent and effective antipsychotic, it has considerable side effects.

Conclusions

Antipsychotic drugs are the first line and mainstay of treatment for schizophrenia. They help to effectively treat psychotic symptoms such as hearing voices and seeing things (hallucinations) and having strange beliefs (delusions). Fluphenazine was one of the first antipsychotics and has been available for around 50 years. Fluphenazine is inexpensive and in developing countries, may be one of the only drug treatments available. In most of Europe and North America, despite still being available, the arrival of newer antipsychotic drugs has reduced the use of fluphenazine and its market share. Fluphenazine has debilitating side effects, including: dizziness; movement disorders such as involuntary movements or spasms; shaking and tremors; inner restlessness and the inability to sit still; and problems with blood pressure, fever and muscle stiffness.

This review included seven studies and compared the effects of fluphenazine taken by mouth with placebo ('dummy' treatment). In the main, the findings of the review support the widespread view that fluphenazine is a potent and effective antipsychotic but has considerable side effects, other antipsychotic drugs may well be preferable. Fluphenazine is an imperfect treatment with serious side effects, so other inexpensive antipsychotic drugs with fewer side effects may be better for people with schizophrenia. Despite this, fluphenazine has a low cost and is widely available, so is likely to remain one of the most widely used treatments for schizophrenia worldwide. However, some of fluphenazine's side effects could be expensive in terms of human suffering and personal cost of treatment. Even though fluphenazine has been used as an antipsychotic drug for decades, there are still a surprisingly small number of well-conducted studies measuring its effectiveness and potential to cause side effects. Future large-scale research should report on important outcomes such as improvement in mental health, relapse, hospital discharge and admission, levels of satisfaction with treatment and quality of life.

This plain language summary has been written by a consumer Ben Gray from RETHINK.