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[Intervention Review]

Increasing antipsychotic dose versus switching antipsychotic for non response in schizophrenia

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ABSTRACT

Background

Many people with schizophrenia do not respond to an initially prescribed antipsychotic drug. In such cases, one treatment strategy could be to increase the antipsychotic dose; and another strategy could be to switch to a different antipsychotic drug.

Objectives

To examine the efficacy of increasing the antipsychotic dose versus switching the antipsychotic drug in the treatment of non-responsive people with schizophrenia.

Search methods

We searched the Cochrane Schizophrenia Group Trials Register (10 June 2014, 6 October 2015, and 30 March 2017). We examined references of all included studies for further trials.

Selection criteria

All relevant randomised controlled trials (RCTs) comparing increasing the antipsychotic dose versus switching to a different antipsychotic drug for people with schizophrenia who have not responded to their initial antipsychotic treatment.

Data collection and analysis

At least two review authors independently extracted data. We analysed dichotomous data using relative risks (RR) and their 95% confidence intervals (CIs). We analysed continuous data using mean differences (MD) and their 95% CIs. We assessed risk of bias for included studies and used GRADE to create a 'Summary of findings' table.

Main results

We include one RCT with relevant data on 29 participants in this review. The trial had a parallel design and was double-blind, but blinding procedures were not described. The trial included people who were non-responsive to fluphenazine 20 mg/day administered for 4 weeks. Participants were randomly assigned to continuing treatment with fluphenazine 20 mg/day, increasing the dose to fluphenazine 80 mg/day or switching to haloperidol 20 mg/day for four additional weeks. Data were reported only for 47 out of 58 initially randomised participants. The trial was published in 1993. The fact that only one RCT with a small sample size (N = 29) was included in the analysis limits the quality of the evidence. Overall, no clear difference was found between groups in terms of the three available outcomes: global state (number of participants with clinically relevant response (RR 1.63, 95% CI 0.17 to 15.99, *very low quality evidence*); general mental state (endpoint



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score, BPRS total) (MD 2.00, 95% CI –4.20 to 8.20, *very low quality evidence*); and negative symptoms (endpoint score, SANS) (MD 3.40, 95% CI –12.56 to 19.36). No data were reported for leaving the study early, adverse effects, time in hospital, quality of life, satisfaction with care and functioning.

Authors' conclusions

There is extremely limited evidence and no clear conclusions can be drawn. There is an urgent need for further trials in order to determine the optimal treatment strategy for people with schizophrenia who do not respond to their initial antipsychotic treatment.

PLAIN LANGUAGE SUMMARY

Increasing antipsychotic dose versus switching to a different antipsychotic for people with schizophrenia who do not respond to initial treatment

Review question

If a person with schizophrenia does not initially respond to an antipsychotic, is increasing the dose of this antipsychotic more effective, and safer, compared with switching to another antipsychotic?

Background

Many people with the serious mental illness schizophrenia do not respond fully (i.e. symptoms such as delusions and hallucinations still remain) with a standard dose of an initially prescribed antipsychotic drug. In such cases, clinicians can consider increasing the antipsychotic dose beyond regular thresholds or switching to a different antipsychotic drug in order to enhance antipsychotic efficacy. The evidence surrounding the optimal treatment strategy is scarce.

Searching for evidence

The Information Specialist of Cochrane Schizophrenia ran an electronic search (up to 30 March 2017) for trials that randomised people with schizophrenia who were not responding to their initial antipsychotic treatment to receive either an increased antipsychotic dose or switch to a different antipsychotic drug. Nine hundred and two records were found and checked by the review authors.

Evidence found

Only one trial met the review requirements and provided usable data. Data were reported for the number of participants who responded to treatment, the general mental state of participants at endpoint of the trial and the presence of negative symptoms at endpoint. There were no data available for any other outcome. No clear difference between increasing the dose of the antipsychotic drug and switching to a different antipsychotic was shown. The available evidence was extremely limited and of very low quality.

Conclusions

The results of the present review show that there is no good-quality evidence to help clinicians decide between increasing the antipsychotic dose or switching to a different antipsychotic drug for people not responding to their initial antipsychotic treatment. Therefore, no clear conclusions can be drawn. Larger, well-designed trials are needed.