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Increasing antipsychotic dose for non response in schizophrenia (Review)

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[Intervention Review]

Increasing antipsychotic dose for non response in schizophrenia

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ABSTRACT

Background

Many people with schizophrenia do not reach a satisfactory clinical response with a standard dose of an initially prescribed antipsychotic drug. In such cases, clinicians face the dilemma of increasing the antipsychotic dose in order to enhance antipsychotic efficacy.

Objectives

To examine the efficacy of increasing antipsychotic dose compared to keeping the same dose in the treatment of people with schizophrenia who have not responded (as defined in the individual studies) to an initial antipsychotic drug trial. We also examine the adverse effects associated with such a procedure.

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), reporting useable data, comparing increasing the antipsychotic dose rather than maintaining the original dose for people with schizophrenia who do not respond 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 the 95% confidence intervals (CI). We analysed continuous data using mean differences (MD) and their 95% CI. We assessed risk of bias for included studies and used GRADE to create a 'Summary of findings' table.

Main results

Ten relevant RCTs with 675 participants are included in this review. All trials were double blind except one single blind. All studies had a run-in phase to confirm they did not respond to their initial antipsychotic treatment. The trials were published between 1980 and 2016. In most studies the methods of randomisation, allocation and blinding were poorly reported. In addition sample sizes were often small, limiting the overall quality of the evidence. Overall, no clear difference was found between groups in terms of the number of participants who showed clinically relevant response (RR 1.09, 95% CI 0.86 to 1.40, 9 RCTs, N = 533, *low-quality evidence*), or left the study early due to adverse effects (RR 1.63, 95% CI 0.52 to 5.07, *very low quality evidence*), or due to any reason (RR 1.30, 95% CI 0.89 to 1.90, 5 RCTs, N = 353, *low-quality evidence*). Similarly, no clear difference was found in general mental state as measured by PANSS total score change (MD –1.44, 95% CI –6.85 to 3.97, 3 RCTs, N = 258, *very low quality evidence*). At least one adverse effect was equivocal between groups (RR 0.91, 95%



CI 0.55 to 1.50, 2 RCTs, N = 191, very low quality evidence). Data were not reported for time in hospital or quality-of-life outcomes. Finally, subgroup and sensitivity analyses did not show any effect on the primary outcome but these analyses were clearly underpowered.

Authors' conclusions

Current data do not show any clear differences between increasing or maintaining the antipsychotic dose for people with schizophrenia who do not respond to their initial antipsychotic treatment. Adverse effect reporting was limited and poor. There is an urgent need for further trials in order to determine the optional treatment strategy in such cases.

PLAIN LANGUAGE SUMMARY

Increasing versus maintaining the dose of antipsychotic medication for people with schizophrenia who do not respond to treatment

Review question

If a person with schizophrenia does not initially respond to an antipsychotic medication, is increasing the dose of this antipsychotic effective and safe?

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 of their specialised register 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 continue on the same dose. The search returned 1919 records, which were checked for eligibility by the review authors.

Evidence found

Ten trials met the review requirements and provided usable data. No clear difference between increasing the dose of the antipsychotic drug and continuing antipsychotic treatment at the same dose was shown for any efficacy (clinical response) or safety (incidence of adverse effects) outcomes. The evidence currently available is limited and of low or very low quality. In particular, very few studies reported adverse effects adequately.

Conclusions

The results of the present review show that there is no good-quality evidence to support or refute the hypothesis that increasing the antipsychotic dose for patients not responding to their initial antipsychotic treatment differs from continuing antipsychotic treatment at the same dose. No clear evidence regarding safety is available. Therefore, no firm conclusions can be made. Larger, well-designed trials are needed.