Effects of the atypical antipsychotic risperidone on hostility and aggression in schizophrenia: a meta-analysis of controlled trials

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Authors' objectives
To evaluate the published evidence regarding the effects of risperidone on hostility and aggression in schizophrenia.

Searching
MEDLINE and PsycLIT were searched from 1990 to June 2000. The search terms were 'risperidone', 'schizophrenia', 'aggression' and 'hostility'.

Study selection
Study designs of evaluations included in the review
Only studies with a controlled design, i.e. placebo-control condition or typical antipsychotic control condition, were included. One trial was of 6 months’ duration, one was 9 weeks, 4 were 8 weeks and one was 4 weeks.

Specific interventions included in the review
Only comparisons of risperidone with another antipsychotic or a placebo were eligible for inclusion. Risperidone was compared with haloperidol in 4 studies, with haloperidol and placebo in 2 studies and with perphenazine in one study. Risperidone was given in doses that ranged from one to 16 mg daily. The doses of the other antipsychotics were only specified for two studies.

Participants included in the review
The authors did not specify any inclusion and exclusion criteria relating to the participants. The demographic and disease characteristics of the participants in the included studies were not reported.

Outcomes assessed in the review
The outcome measures of hostility and aggression that were specified for inclusion were ratings on the hostility item(s) of standardised psychiatric rating scales, such as the Brief Psychiatric Rating Scale and the Positive and Negative Syndrome Scale (PANSS), and reports of the number of seclusions and restraints. Five of the included studies used PANSS, one used reports of seclusions and restraints, and another used the Psychiatric Anxiety Scale.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
Quality was not formally assessed, although the authors identified 'studies of rigorous methodology' on the basis of whether they were double-blind and used random assignment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. The abstracted data were the number of participants in the intervention and control group, study design (including randomisation and blinding), risperidone dosage, trial duration, and type of hostility and aggression measure used. The authors calculated Cohen's d: the difference between the mean of the experimental group and the mean of the comparison group, divided by the pooled standard deviation (see Other Publications of Related Interest).
Methods of synthesis
How were the studies combined?
The authors state that meta-analytic methods were used to obtain a combined effect size, to indicate the magnitude of the association across all the studies. The effect sizes were weighted for sample size. Stoufer's Z, weighted for sample size, was used to provide an indication of the difference between the patient and the comparison group. For those studies that indicated there was no significant difference between the experimental and control groups, but did not provide further statistical information, a 'd' of 0.00 was used.

How were differences between studies investigated?
An overall analysis was carried out in which all of the studies were included. In a second analysis, only those groups that received risperidone dosages of greater than 2 mg daily were included. The third analysis was restricted to studies with a double-blind design and randomised assignment of patients, as well as a risperidone dose of greater than 2 mg. A final analysis was carried out on the studies with PANSS hostility rating as an outcome measure and a drug dosage greater than 2 mg/day.

Results of the review
Seven studies (n=2,208) were included. Five studies (n=1,648) were double-blind with random assignment; one of the remaining studies (n=101) was double-blind, but the original paper did not indicate whether patient assignment was randomised; the remaining study (n=27) was not double-blind and did not have random assignment.

When all the studies were included, risperidone was significantly more effective than the other antipsychotics and placebo. For risperidone versus classical antipsychotics (7 studies, n=2,089), d was 0.17 (95% confidence interval, CI: 0.01, 0.34) and Z was 2.11 (p=0.02); for risperidone versus placebo (2 studies, n=456), d was 0.28 (95% CI: 0.07, 0.49) and Z was 2.65 (p=0.004).

When the analysis was restricted to those participants who received a risperidone dosage greater than 2 mg, risperidone was significantly more effective than the other antipsychotics and placebo. For risperidone versus classical antipsychotics (7 studies, n=1,776), d was 0.29 (95% CI: 0.07, 0.51) and Z was 2.57 (p=0.005); for risperidone versus placebo (2 studies, n=456 participants), d was 0.31 (95% CI: 0.10, 0.53) and Z was 2.91 (p=0.002).

When the analysis was restricted to double-blind studies with random assignment and a dosage greater than 2 mg, risperidone was significantly more effective than the other antipsychotics and placebo. For risperidone versus classical antipsychotics (3 studies, n=1,648) d was 0.37 (95% CI: 0.21, 0.52) and Z was 4.61 (p<0.0001).

When the analysis was restricted to studies using a PANSS outcome measure and drug dosage greater than 2 mg, risperidone was significantly more effective than the other antipsychotics (5 studies, n=1,708): d was 0.39 (95% CI: 0.21, 0.57) and Z was 4.25 (p<0.0001).

Authors' conclusions
Risperidone is superior to classical antipsychotics and placebo in the treatment of hostility and aggression in schizophrenia.

CRD commentary
The authors set out a clearly defined review question and the inclusion criteria were clearly specified for the outcome measures and study design. However, the inclusion and exclusion criteria relating to the participants were not specified, and the characteristics of the participants in the included studies were not provided. Consequently, it is not possible to assess the heterogeneity between the studies, or to assess the possible applicability of the findings in terms of characteristics such as age and type of schizophrenia. Details on the dose of the alternative antipsychotics were only provided for two of the studies. Therefore, it is not possible to assess the possible impact that this may have had on variability between the studies.

The literature search was restricted to two databases; there was no mention of checking the references from retrieved...
articles and there was no attempt to identify unpublished studies. It is unlikely that all relevant research was identified. Publication bias was not assessed. A formal assessment of the methodological quality of the included studies was not reported. The authors did, however, carry out a separate analysis that included only double-blind randomised trials. Other possible sources of methodological bias were not considered.

Some details of the individual studies were presented, although the tables of data could have been more comprehensive. The limited information on the individual studies makes it difficult to assess the possible reasons for the variability in effect sizes and, therefore, the appropriateness of using standardised mean differences. The exact effect sizes or 95% CIs for the individual studies were not presented. Also, there was no information on the statistical model used to pool the effect sizes. A systematic assessment of heterogeneity was not carried out, although the authors did examine the effect of methodological differences between the studies.

The authors’ conclusions are overconfident considering the lack of information on how this review was conducted, the limited search, the lack of study details and the pooling of heterogeneous data.

**Implications of the review for practice and research**

**Practice:** The authors state that risperidone may be useful in the treatment of aggression and hostility in schizophrenia and, based on other recent studies not included in the review, in the treatment of other psychiatric conditions.

**Research:** The authors state that the conclusions from this review need to be confirmed by controlled double-blind studies in various patient populations. In addition, they suggest that future research should make use of specific rating scales that have been developed for the assessment of different aspects of hostility and aggression, which they claim will strongly improve the reliability and validity of such measures.

**Bibliographic details**

Aleman A, Kahn R S. Effects of the atypical antipsychotic risperidone on hostility and aggression in schizophrenia: a meta-analysis of controlled trials. European Neuropsychopharmacology 2001; 11(4): 289-293

**PubMedID**

11532383

**Other publications of related interest**


**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Aggression /drug effects /psychology; Antipsychotic Agents /pharmacology /therapeutic use; Controlled Clinical Trials as Topic; Hostility; Humans; Risperidone /pharmacology /therapeutic use; Schizophrenia /drug therapy; Schizophrenic Psychology

**AccessionNumber**

12001006160

**Date bibliographic record published**

31/05/2003

**Date abstract record published**

31/05/2003
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.