Meta-analytic study of the benefits and risks of treating chronic schizophrenia with risperidone or conventional neuroleptics


Authors' objectives
To assess the benefits and the risks of treating chronic schizophrenia with risperidone or conventional neuroleptics.

Searching
Not stated. Publication dates of included studies ranged from 1992 to 1995.

Study selection
Study designs of evaluations included in the review
Double-blind randomised controlled trials (RCTs). Follow-up ranged from 4 to 12 weeks. An intention-to-treat (last observation carried forward) analysis was performed.

Specific interventions included in the review
Risperidone (fixed dosage of 4mg/day; mean dosage range 6 to 12.0mg/day), conventional neuroleptics (haloperidol (fixed dosage 10-20 mg/day; mean dosage range 9.2 to 10.3mg/day) zuclopenthixol (mean dosage 38.0mg/day) and perphenazine (mean dosage 28.0mg/day)) or placebo. Studies that included the active control drug haloperidol at doses that exceeded 20mg/day were excluded. In dose finding trials only one of the fixed doses used was considered to avoid statistical problems with homogeneity.

Participants included in the review
Patients with chronic schizophrenia as measured by DSM-III-R criteria (see Other Publications of Related Interest). The mean age range was 34 to 38 years. The total male/female ratio was 624:287.

Outcomes assessed in the review
Only studies that assessed efficacy and risk of treatment by means of the Positive and Negative Syndrome Scale (PANSS) and the Extrapyramidal Symptom Rating Scale (ESRS) were included in the review. The PANSS scores on three subscales (positive symptoms, negative symptoms and general psychopathology) which were included separately in the review. Studies were also required to provide information on patients' use of antiparkinsonian drugs. Treatment of efficacy in included studies was assessed by several scales including the PANSS, the Brief Psychiatric Rating Scale, and the Clinical Global Improvement Scale. Treatment safety was also assessed by questionnaire on adverse events and patients' spontaneous reports of adverse events.

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
The authors do not report the method used to assess quality, or how the quality assessment was performed.

Data extraction
The authors do not state how data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The effect size for the PANSS was defined as the mean change in the scale score (baseline to end point) for patients
treated with risperidone minus the mean change score for the patients treated with the neuroleptic, divided by the pooled standard deviation (SD) of the two treatment groups. For the ESRS, the effect size was defined as the mean change in the scale score (baseline to worst score) for patients treated with the neuroleptic minus the mean change score for patients treated with risperidone divided by the pooled SD of the two treatment groups. The effect size for the percentage of patients receiving antiparkinsonian drugs was estimated using the transformations of proportions.

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.

Results of the review
Six RCTs (911 patients, 457 received risperidone and 454 conventional neuroleptics).

Efficacy: Effect size (ES) for positive symptoms of individual studies ranged from 0.04 to 0.62 with an overall ES (for all trials) of 0.33. The ES of individual studies for negative symptoms ranged from 0.08 to 0.49 with an overall ES of 0.22. The ES of individual studies for the general psychopathology subscale ranged from 0.05 to 0.63 with an overall ES of 0.37.

Safety (results from six RCTs): The ES of individual studies for scores on the questionnaire ranged from -0.05 to 0.46 with an overall ES of 0.31. The ES of individual studies for total ESRS ranged from 0.03 to 0.52 with an overall ES of 0.36. The ES of individual studies for Dystonia ranged from 0.03 to 0.35 with an overall ES of 0.18. The ES of individual studies for parkinsonism ranged from 0.01 to 0.56 with an overall ES of 0.31. The ES of individual studies for antiparkinsonian ranged from 0.20 to 0.63 with an overall ES of 0.37. Antiparkinsonian drugs were taken by 20% of the risperidone patients and by 38% receiving conventional neuroleptics.

Authors' conclusions
These data indicate that risperidone is a more effective antipsychotic that the conventional agents and causes less severe extrapyramidal symptoms.

CRD commentary
The review included a clearly specified inclusion/exclusion criteria. No information is presented on the literature search or how decision on the relevance of primary studies was conducted therefore both selection and publication bias may be present. No information is presented on the quality assessment of included studies, however, only double blind randomised controlled trials were included in the review. No assessment of heterogeneity of included studies was performed and therefore it is not possible to assess the appropriateness of pooling the results. Selection bias may exist because the authors select only one from several fixed doses of risperidone in three large trials. The overall effect size was estimated by simple pooling without weighting by individual study's precision or sample size. Thus the treatment effect has been over estimated because smaller studies tend to report larger effect sized. This may be a meta-analysis sponsored by a drug company.

Therefore the authors' conclusions should be interpreted with great caution owing to the above limitations.

Implications of the review for practice and research
The authors did not state any implications for further research and practice.

Bibliographic details

Other publications of related interest

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Subject indexing assigned by CRD

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**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.