Review: risperidone produces more clinical improvement and causes fewer extrapyramidal side effects in schizophrenia

Kennedy E, Song F, Hunter R, et al. *Risperidone versus 'conventional' antipsychotic medication for schizophrenia*. In: *the Cochrane Database of Systematic Reviews* [updated 29 August 1997]. In the Cochrane Library [database on disk and CD-ROM]. The Cochrane Collaboration; issue 4. Oxford: Update Software, 1997.

Objective

To evaluate the effectiveness, using meta-analysis, of risperidone compared with "conventional" neuroleptic drugs in patients with schizophrenia.

Data sources

Studies were identified using Medline, Biological Abstracts, Embase, PsycLIT, and the Cochrane Library; reviewing the references of published studies; and contacting pharmaceutical companies for data on unpublished trials.

Study selection

Studies were selected if they were randomised controlled trials that compared risperidone with other conventional neuroleptic agents (haloperidol in 10 studies) for schizophrenia or schizophrenia like psychosis (schizophreniform and schizoaffective disorders).

Data extraction

Data were extracted on patient characteristics, diagnosis and duration of illness, antipsychotic drug types, and dosages. Main outcome measures were clinical improvement (measured as: (1) 20% reduction in total score on the Positive and Negative Symptom Rating Scale (PANSS) or the Brief Psychiatric Rating Scale (BPRS); 1 study used a 50% reduction in total PANSS score; (2) "clinically improved" on the Clinical Global Impression (CGI) scale), extrapyramidal side effects (EPS), and acceptability of treatment (drop out rate).

Main results

12 studies (2696 patients) (mean age 37 y, 70% men, mean time since onset of symptoms 15 y, mean of 6 previous admissions) met the inclusion criteria. 1857 patients received risperidone, 574 received haloperidol, 123 received other conventional neuroleptics, and 142 received placebo. Risperidone led to greater

clinical improvement when measured by the PANSS and BPRS (10 studies) [$p < 0.003$]* but not by the CGI scale (6 studies) [$p = 0.13$]* (table). Fewer patients who received risperidone had EPS (8 studies) [$p < 0.001$]* and the drop out rate was reduced with risperidone (12 studies) [$p = 0.005$]* (table).

Conclusion

Risperidone produces greater clinical improvement than conventional neuroleptic agents in patients with schizophrenia and is associated with fewer extrapyramidal side effects.

*p values calculated from data in article.

Risperidone v conventional neuroleptics†

Outcomes	Risperidone weighted EER	Neuroleptics weighted CER	RBI (95% CI)	Weighted ABI	NNT (CI)
Clinical improvement					
PANSS/ BPRS	58.6%	51.4%	14% (4 to 24)	7.2%	14 (9 to 41)
CGI scale	62%	57.3%	9% (-2 to 24)	4.7% (CI -1.3 to 10.6)	NS
Outcomes	Risperidone weighted EER	Neuroleptics weighted CER	RRR (CI)	Weighted ARR	NNT (CI)
EPS	28%	42.5%	37% (24 to 55)	14.5%	7 (6 to 10)
Dropout rate	27.7%	33.4%	18% (7 to 28)	5.7%	18 (11 to 58)

† CGI = clinical global impression; EPS = extrapyramidal side effects; PANSS = Positive and Negative Symptom Rating Scale; BPRS = Brief Psychiatric Rating Scale; NS = not significant. Other abbreviations defined in glossary; RBI, ABI, RRR, ARR, NNT, and CI calculated from data in article.

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Commentary

The review by Kennedy *et al* provides useful information on the effectiveness of risperidone compared with conventional neuroleptics (mainly haloperidol) in patients with chronic schizophrenia. The reviewers increased the robustness of their conclusions by including only randomised controlled trials. One of the main contributions of the review is to highlight the clear limitations of the primary studies. Most of the trials studied patients for < 12 weeks and all but 1 trial randomised only patients with chronic schizophrenia and used a cut off of 20% in rating scales (BPRS and PANSS) to measure improvement. No suitable information regarding clinically meaningful outcomes such as relapse, hospitalisation,

quality of life, social functioning, or employment status of the patients was provided by the original trials. The absence of cost data precluded an analysis of the cost effectiveness of risperidone. Additionally, although risperidone seems to cause fewer EPS, this medication was compared with a fixed or high dose of haloperidol (which may be more likely to cause EPS than other conventional neuroleptics), and specific information about drug induced movement disorders was given in only 2 trials.^{1 2}

Risperidone seems to improve the clinical symptoms of patients with chronic schizophrenia in the short term (< 12 weeks), causes fewer EPS, and leads to less discontinuation. However, 14 patients

must be treated with risperidone, rather than haloperidol, for 1 additional patient to achieve a 20% reduction in BPRS or PANSS score. It is unclear whether this result is clinically meaningful or if such results will remain the same over a long term treatment period. Doubts remain regarding the cost effectiveness of this medication and no clear statement can be made about its effect on the positive or negative symptoms of schizophrenia.

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