Haloperidol dose for the acute phase of schizophrenia: a Cochrane review

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Background
Haloperidol is an accessible benchmark antipsychotic against which the effects of newer treatments are gauged.

Objectives
The primary goal of this review is to determine the best range of doses of haloperidol for the treatment of people acutely ill with schizophrenia.

Search strategy
• References of all included studies
• Industry

Criteria
Study methods
Randomised trials.

Participants
People with schizophrenia or schizophrenia-like illnesses, diagnosed by any criteria.

Interventions
One dose of haloperidol vs another dose of haloperidol – categories of dose were stipulated before seeing data. We included any means of administration except depot.

Drug dosages
1. Haloperidol: > 0.25 - 1.5 mg/day (ultra low dose)
2. Haloperidol: > 1.5 - 3.0 mg/day (low dose)
3. Haloperidol: > 3.0 - 7.5 mg/day (standard-lower dose)
4. Haloperidol: > 7.5 - 15 mg/day (standard-higher dose)
5. Haloperidol: > 15 - 35 mg/day (high dose)
6. Haloperidol: > 35 mg/day (very high dose)

Plasma levels
1. Haloperidol: > 1.4-3.5ng/ml (very low plasma levels)
2. Haloperidol: > 3.5-7mg/ml (low plasma levels)
3. Haloperidol: > 7.0-16.5 ng/ml (medium plasma levels)
4. Haloperidol: > 16.5ng/ml (high plasma levels)

Data collection & analysis
We independently inspected citations and extracted data.

We calculated relative risk (RR), 95% confidence interval (CI) and the number needed to treat (NNT) on an intention-to-treat basis.

Results
We included 16 trials, from between 1967 and 2000, with 19 different randomised dose comparisons.

The largest study involved 132 people, the smallest only 20.

No studies reported data on relapse rates or quality of life and none compared >1.5-3.0 mg/day haloperidol to higher dose ranges.

Using low doses (>3-7.5mg/day) did not clearly result in loss of efficacy, although data are surprisingly sparse.

Haloperidol doses in the range of >3-7.5 mg/day had a somewhat lower rate of clinically significant extrapyramidal adverse effects than higher doses.

Rates of extrapyramidal adverse effects were, however, high whatever the dose.

The results from this review1 are in keeping with other relevant Cochrane reviews2.

Using haloperidol in modern randomised trials ensures that the control group participants benefit from antipsychotic effects but also exhibit adverse effects against which most comparison drugs will compare favourably.

All other outcomes within the several comparisons shown below did not yield statistically significant differences.

Several, particularly with lower dose ranges, were underpowered to detect meaningful differences.

Conclusions
No results are conclusive. All are based on small, short, studies.

It would be understandable, however, if clinicians were cautious to prescribe doses in excess of 7.5 mg/day of haloperidol to people with uncomplicated acute schizophrenia, and if people with schizophrenia were equally reticent to take greater doses.

Further research is needed regarding the efficacy and tolerability of the >1.5-3.0 mg/day dose range.

7-10mg haloperidol/day is equally clinically effective (with a different, more problematic, adverse effect profile) to many new atypicals, chlorpromazine, sulpiride or even trifluoperazine.

Considering the prevalence of adverse effects haloperidol is not the best control drug for use in fair randomised studies.

References

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