Therapeutics EBM Volume 7 May/June 2002 89

Review: haloperidol does not reduce agitation in dementia


QUESTION: In patients with dementia, is haloperidol effective for decreasing agitation?

Data sources
Studies were identified by searching the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group, which contains records from 15 databases. Pharmaceutical companies and authors were contacted.

Study selection
2 reviewers independently selected studies in any language if they were randomised, placebo controlled trials with allocation concealment and assessment of agitation before and after treatment; if they involved patients who had dementia (unclassified or diagnosed according to criteria) and agitation and treatable causes were ruled out; and if they evaluated haloperidol for > 1 week.

Data extraction
Reviewers assessed the quality of studies and extracted data on patient and study characteristics, interventions, and outcomes (the main outcome was decrease in manifestations of agitation).

Main results
5 studies (876 patients, mean age range 72 to 82 y, 56% to 67% women) met the selection criteria. 3 studies included outpatients, and 2 studies included institution-alised patients. Treatment duration ranged from 3 to 16 weeks (mean 8.6 wks). Mean doses were categorised as < 2 mg/day and > 2 mg/day (range 0.5 to 6.0 mg/d). In patients with mild or moderate dementia (Mini-Mental State Examination score 12 to 19), the groups did not differ for agitation or global improvement (table) on any type of measure or dose. Haloperidol, mean dose > 2 mg/day, led to a greater reduction in aggression (2 studies, standardised mean difference in change from baseline score 0.37, 95% CI 0.11 to 0.62) and to more adverse events.

CGIC improvement at 3 to 4 weeks

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Dose</th>
<th>Hal</th>
<th>Placebo</th>
<th>RBI (95% CI)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGIC improvement at 3 to 4 weeks</td>
<td>&gt; 2 mg/day</td>
<td>79%</td>
<td>69%</td>
<td>15% (~2.4 to 36)</td>
<td>Not significant</td>
</tr>
<tr>
<td>CGIC improvement at 16 weeks</td>
<td>&lt; 2 mg/day</td>
<td>32%</td>
<td>31%</td>
<td>5.9% (~47 to 110)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Drop outs because of adverse events by 3 to 6 weeks</td>
<td>&gt; 2 mg/day</td>
<td>17%</td>
<td>5.8%</td>
<td>189% (23 to 589)</td>
<td>10 (5 to 41)</td>
</tr>
<tr>
<td>&gt; 1 extrapyramidal symptom by 3 to 6 weeks</td>
<td>&gt; 2 mg/day</td>
<td>34%</td>
<td>17%</td>
<td>93% (18 to 219)</td>
<td>7 (4 to 24)</td>
</tr>
</tbody>
</table>

Haloperidol (Hal) v placebo for moderate or mild dementia*

Haloperidol (Hal) v placebo for moderate or mild dementia*

Conclusion
In patients with dementia, haloperidol reduces aggression but does not reduce agitation and increases some adverse events.

COMMENTARY
The review by Lonergan et al is a valiant attempt to draw some useful conclusions from a disparate group of studies of haloperidol in dementia. Only 5 studies could be included; which amounted to < 300 patients on active treatment. Because of a plethora of outcome variables, the subanalyses reduced the numbers even more. An adequate placebo controlled study of haloperidol may no longer be ethical, so gleaning what little information we can from available data has some merit. The authors conclude that haloperidol has some benefit in aggression rather than in the blanket area of agitation.

In patients with dementia, haloperidol reduces agitation but does not reduce agitation and increases some adverse events.

NOTE: Due to page limitations, the commentary is shortened. For further details, please refer to the original publication.