Clonidine and methylphenidate were effective for attention deficit hyperactivity disorder in children with comorbid tics

QUESTION: In children with attention deficit hyperactivity disorder (ADHD) and Tourette’s syndrome (TS), what is the effect of clonidine (CLON), methylphenidate (MPH), or combined CLON and MPH?

Design
Randomised (allocation concealed*), blinded (all parties)†, placebo controlled trial with 16 weeks of follow up.

Setting
11 sites in the US.

Patients
136 children between 7 and 14 years of age (mean age 10 y; 85% boys) who met DSM-IV criteria for ADHD of any subtype and DSM-IV criteria for TS, chronic motor tic disorder, or chronic vocal tic disorder. Exclusion criteria included secondary tic disorder, major depression, pervasive developmental disorder, autism, mental retardation, eating disorders, and medical disorders precluding MPH or CLON use. Follow up was 80%.

Main outcome measures
Severity of ADHD symptoms (Conners Abbreviated Symptom Questionnaire for teachers [ASQ-Teacher]), tic severity (Yale Global Tic Severity Scale [YGTSS]), and global functioning (Children’s Global Assessment Scale [CGAS]).

Main results
CLON (used alone or with MPH) compared with no MPH, and combined CLON and MPH compared with placebo showed beneficial effects for ADHD symptoms as measured by the ASQ-Teacher; the greatest benefit was seen with combined CLON and MPH (table). Combined CLON and MPH was most effective for lessening tic severity and improving global functioning, but CLON or MPH alone was also effective.

Conclusion
Clonidine or methylphenidate used alone and especially in combination were effective for attention deficit hyperactivity disorder in children with comorbid tics.

*See glossary.
†Information provided by author.

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Clonidine (CLON), methylphenidate (MPH), combined CLON and MPH, and placebo in children with attention deficit hyperactivity disorder (ADHD) and comorbid tics.

<table>
<thead>
<tr>
<th>Outcomes at 16 weeks</th>
<th>Comparisons</th>
<th>Treatment effects (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD measured by Conners Abbreviated Symptom Questionnaire for Teachers</td>
<td>CLON v no CLON</td>
<td>3.2 (1.2 to 5.2)</td>
<td>0.002</td>
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<tr>
<td></td>
<td>MPH v no MPH</td>
<td>3.2 (1.1 to 5.2)</td>
<td>0.003</td>
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<tr>
<td>Tic severity measured by the Yale Global Tic Severity Scale</td>
<td>CLON v no CLON</td>
<td>6.3 (2.8 to 9.8)</td>
<td>&lt;0.0001</td>
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<td>MPH v no MPH</td>
<td>4.8 (0.4 to 9.9)</td>
<td>0.07§</td>
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<tr>
<td></td>
<td>CLON + MPH v placebo</td>
<td>11.0 (2.1 to 19.8)</td>
<td>0.003</td>
</tr>
<tr>
<td>Symptom Questionnaire</td>
<td>MPH v no MPH</td>
<td>7.7 (3.4 to 11.9)</td>
<td>0.0005</td>
</tr>
<tr>
<td></td>
<td>CLON + MPH v placebo</td>
<td>14.5 (7.2 to 21.9)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

†Positive values show a beneficial effect of the medication. §Not significant.

COMMENTARY
The well designed trial by the Tourette’s Syndrome Study Group addresses a number of questions related to treating ADHD in patients with tics. The differential effects of CLON and MPH were as follows: (i) MPH provides a broader therapeutic coverage of ADHD symptoms; (ii) MPH is superior to CLON in treating cognitive symptoms of inattention; (iii) CLON provides complementary benefit for treating hyperactive and impulsive behaviours; and (iv) combined CLON and MPH has the greatest effect on global functioning. With respect to adverse effects, combined CLON and MPH was most effective for lessening tic severity; yet, more patients receiving MPH alone reported impulsive behaviours; and (iv) combined CLON and MPH has the greatest effect on global functioning. With respect to adverse effects, combined CLON and MPH was most effective for lessening tic severity; yet, more patients receiving MPH alone reported impulsive behaviours; and (iv) combined CLON and MPH has the greatest effect on global functioning. With respect to adverse effects, combined CLON and MPH was most effective for lessening tic severity; yet, more patients receiving MPH alone reported impulsive behaviours; and (iv) combined CLON and MPH has the greatest effect on global functioning.