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 [patients, clinicians, data collectors, outcome assessors, data analysts, data safety and monitoring committee, and manuscript writers]**†, 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 had ADHD of any subtype and TS, chronic motor tic disorder, or chronic vocal tic disorder. Exclusion criteria included secondary tic disorder, major depression, pervasive developmental disorder, autism, mental retardation, anorexia nervosa, and bulimia. Follow up was 80%.

**Intervention**

Children were allocated to receive CLON alone (n=34), MPH alone (n=37), combined CLON and MPH (n=33), or placebo (n=32). Weeks 1 to 4 were a dosage titration period for CLON (0.1 mg tablets or matching placebo). Children continued to receive CLON (or placebo) during weeks 5 to 8, which was the dosage titration period for MPH (5 mg capsules or matching placebo).

**Main outcome measures**

Severity of ADHD symptoms measured by the Conners Abbreviated Symptom Questionnaire for Teachers (ASQ-Teacher), tic severity measured by the Yale Global Tic Severity Scale (YGTTSS), and global functioning measured by the Children’s Global Assessment Scale (C-GAS).

**Main results**

Results are in the table. CLON (used alone or with MPH) compared with no CLON, MPH (used alone or with CLON) 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, which 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, was effective for attention deficit hyperactivity disorder in children with comorbid tics.

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**For correspondence:** Dr R Kurlan, University of Rochester Medical Center, Rochester, New York, USA. roger_kurlan@urmc.rochester.edu.

**Abstract and commentary also appear in Evidence-Based Mental Health.**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Comparisons</th>
<th>Treatment effects (95% CI)</th>
<th>p Value</th>
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</thead>
<tbody>
<tr>
<td>ADHD (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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<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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<td>CLON + MPH v placebo</td>
<td>6.3 (2.8 to 9.8)</td>
<td>&lt; 0.0001</td>
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<tr>
<td>Tic severity (Yale Global Tic Severity Scale)</td>
<td>CLON v no CLON</td>
<td>6.2 (1.1 to 11.3)</td>
<td>0.02</td>
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<td></td>
<td>MPH v no MPH</td>
<td>4.8 (4.0 to 9.9)</td>
<td>0.071</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>
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<tr>
<td>Global functioning (Children’s Global Assessment Scale)</td>
<td>CLON v no CLON</td>
<td>6.9 (2.7 to 11.1)</td>
<td>0.002</td>
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<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>
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</tbody>
</table>

*Positive values show a beneficial effect of the medication.

**COMMENTARY**

The well designed trial by the Tourette’s Syndrome Study Group addresses various questions related to treating ADHD in patients with tics. In terms of treatment effectiveness, CLON, MPH, and combined CLON and MPH were all more effective than placebo for treating symptoms of ADHD, and the greatest treatment effect was seen with combined CLON and MPH. The differential effects of CLON and MPH on symptoms of ADHD were as follows: MPH provides a broader therapeutic coverage of ADHD symptoms; CLON is superior to MPH in treating tics at 16 weeks. Tics were not substantially worsened in the treatment group when combined CLON and MPH were used, while MPH alone was more effective for improving tic severity. The study excluded patients with known cardiac problems. Thus, the safety of combined CLON and MPH in this group was not addressed.

The study supports the effectiveness and safety of MPH, CLON, or the 2 drugs combined for treating symptoms of ADHD in children with tics. Tics were not substantially worse in the treatment group than in the placebo group. Further, the study did not address the relation of MPH dose and the emergence of tics, which is an important clinical issue. This study agrees with other reports on the safety of using MPH and CLON. However, careful history, examination, and monitoring are still warranted.

J Goldberg, MB, FRCP, McMaster University Hamilton, Ontario, Canada


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