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

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The Tourette's Syndrome Study Group. *Treatment of ADHD in children with tics: a randomized controlled trial. Neurology* 2002 Feb 26;58:527–36.

**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 86%.

## 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 1–4 were a dosage titration period for CLON (0.1 mg tablets). Children continued to receive CLON (or placebo) during weeks 5–8, which was the dosage titration period for MPH (5 mg capsules).

## 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 [C-GAS]).

## Main results

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 (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.

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

Outcomes at 16 weeks	Comparisons	Treatment effects (95% CI)	p Value
ADHD measured by Conners Abbreviated Symptom Questionnaire for Teachers	CLON v no CLON	3.2 (1.2 to 5.2)	0.002
	MPH v no MPH	3.2 (1.1 to 5.2)	0.003
	CLON + MPH v placebo	6.3 (2.8 to 9.8)	<0.0001
Tic severity measured by the Yale Global Tic Severity Scale	CLON v no CLON	6.2 (1.1 to 11.3)	0.02
	MPH v no MPH	4.8 (–0.4 to 9.9)	0.07§
	CLON + MPH v placebo	11.0 (2.1 to 19.8)	0.003
Global functioning measured by the Children's Global Assessment Scale	CLON v no CLON	6.9 (2.7 to 11.1)	0.002
	MPH v no MPH	7.7 (3.4 to 11.9)	0.0005
	CLON + MPH v placebo	14.5 (7.2 to 21.9)	<0.0001

‡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 coverage of ADHD 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 tics as a reason for limiting further increases in their MPH dose. However, the reported frequency of tic worsening was the same across all treatments, which is supportive of other studies.<sup>1</sup> CLON alone or in combination with MPH was not associated with adverse cardiac effects, but the study excluded patients with known cardiac problems and thus the safety of combined CLON and MPH was not addressed.

This study supports the effectiveness and safety of MPH, CLON, or the 2 drugs in combination for treating symptoms of ADHD in children with tics. Tics were not substantially worse in the treatment group than the placebo group; however, the duration of the trial (16 wks) is insufficient to determine the long term safety of MPH for tics. Furthermore, the study does not address the relation of MPH dose and the emergence of tics, which is an important clinical issue.<sup>2</sup> This study is in agreement with other reports on the safety of using MPH and CLON. However, careful history, examination, and monitoring are still warranted at this time.<sup>3,4</sup>

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