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ATTENTION DEFICIT & COMORBID DISORDERS

ADHD & TOURETTE SYNDROME

The efficacy of methylphenidate (MPH) and clonidine (CLON), alone and in combination, in 136 children with attention deficit hyperactivity disorder (ADHD) and chronic tic disorder, was evaluated in a multicenter, randomized, double-blind clinical trial, and reported by the Tourette Syndrome Study Group from the University of Rochester, NY. Patients assigned to one of 4 groups received MPH (average dose, 27.5 mg/d) alone (37 children), CLON (0.25 mg/d) alone (34), CLON (0.28 mg/d) + MPH (26.1 mg/d) combined (33), or placebo (32). The 16 week trial consisted of CLON/placebo dose titration (weeks 1-4), MPH/placebo dose titration (weeks 5-8), and maintenance therapy (weeks 9-16). Several rating scales were employed at base-line, including Parent and Teacher Conners Questionnaires for ADHD, and site investigator, teacher, and parent scales for tic severity and frequency. Using the Conners Abbreviated Symptom Questionnaire (Teacher) as the ADHD primary outcome measure, compared to placebo, the CLON and MPH treated patients were improved in 60% and 80%, respectively ($p < .002$ and $p < .003$). The greatest improvement (85%) occurred in the combined CLON + MPH-treated patients ($p < .0001$). Impulsivity and hyperactivity were controlled most effectively by CLON, and inattention responded best to MPH. Tic disorder, assessed by the parent/teacher Global Tic Rating and Self Report Scales, was worsened in 20% of MPH-treated subjects (limiting dosage increase in 35%), 26% of those receiving CLON alone, and 22% of the placebo group. A lessening of tic severity, as measured by the investigator-completed Yale Global Scale, occurred in all active treatment groups (CLON + MPH, CLON alone, MPH alone), in that order, when compared with placebo. Sedation was reported in 48% (moderate to severe in 28%) of CLON-treated patients, compared with 14% for MPH alone and 6% for placebo. Cardiac toxicity, necessitating withdrawal from the study, was observed in one subject who developed ECG evidence of isorhythmic dissociation while receiving CLON alone. Patients receiving MPH alone had the lowest rate of side effects. (The Tourette Syndrome Study Group. Treatment of ADHD in children with tics. A randomized controlled trial. *Neurology* February (2 of 2) 2002;58:527-536). (Reprints: Dr Roger Kurlan, Dept of Neurology, University of Rochester Medical Center, Rochester, NY 14642).

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COMMENT. ADHD is frequently associated with tics/Tourette syndrome, occurring in 50% of TS patients (Ped Neur Briefs Nov 2001), and often causing more disability than the tics (Spencer et al, 1995). Neurobiologically, the two disorders appear to be independent (Baumgardner et al, 1996; Ped Neur Briefs Jan 2002;16:6-7), but etiologically, the precipitation or exacerbation of tics in patients with ADHD is often attributed to treatment with central nervous system stimulants, especially methylphenidate (MPH) (Denckla et al,1976; Millichap, 1999). Tics occurring during MPH treatment are dose related, occurring mainly with larger doses.

Despite the evidence linking TS to MPH, recent studies have tended to minimize the risk and causal relationship (Law, Schachar, 1999). In the present placebo-controlled study and report, the authors conclude that their findings fail to support recommendations to avoid MPH in children with ADHD and co-morbid tic disorder. Symptoms of ADHD are benefited by MPH to the same degree as that generally observed in subjects with primary ADHD. A worsening of tics during MPH therapy, that limits an increase in dosage in more than one third, is not significantly different from that observed during treatment with placebo or clonidine. Notwithstanding the rare reports of cardiac irregularities and fatalities following the combined use of MPH and clonidine in the treatment of comorbid ADHD and tics/Tourette syndrome, the authors advocate further trials of combination therapies.

Statistically, these findings are impressive and favor the acceptability of stimulant use in children with ADHD and tics/TS (Nass R, Bressman S. Editorial. *Neurology* 2002;58:513-514). The addition of clonidine to stimulant therapy remains controversial, and is best decided on an individual basis (Nass, Bressman, 2002) or avoided, pending prospective and cardiac monitored, long-term studies. In practice, it is prudent to monitor for tics during treatment of ADHD with stimulant medications, and if treatment is considered essential, dosage should be conservative in patients with a history of co-morbid tics/TS (Millichap JG. Attention Deficit Hyperactivity and Learning Disorders PNB, 2001).

Movement control of manipulative tasks in patients with Gilles de la Tourette syndrome is deranged, in studies of force regulation during action patterns, and functional imaging of secondary motor areas. (Serrien DJ et al. Brain Feb 2002;125:290-300).

SLEEP-DISORDERED BREATHING AND SYMPTOMS OF ADHD

The frequency of sleep-disordered breathing (SDB) among children with inattention and hyperactivity was determined in 866 patients, aged 2.0 to 13.9 years (mean; 6.8 yrs), evaluated in two general pediatric clinics at the University of Michigan and University of Pittsburg. A Pediatric Sleep Questionnaire, for snoring, sleepiness, and risk of SDB, and two behavioral measures (an inattention/hyperactivity scale (IHS) from DSM-IV, and the hyperactivity index (HI) of the Conners' Parent Rating Scale) were completed on each patient. Habitual snoring was associated with a high IHS score (>1.25), and showed a significant association with a high HI score (>60), reflective of hyperactive behavior; 22% of habitual snorers had HI>60, whereas only 12% of nonhabitual snorers had HI>60. Snoring, daytime sleepiness, and SDB scores showed significant associations with IHS and HI. The link between snoring and behavior was strongest for young boys <8 years old. In contrast, sleepiness and SDB showed similar associations in all age- and sex-defined groups. (Chervin RD, Archbold KH, Dillon JE, et al. Inattention, hyperactivity, and symptoms of sleep-disordered