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MOVEMENT DISORDERS

TICS, METHYLPHENIDATE, AND ADHD

The effects of methylphenidate (MPH) on the frequency and severity of tics in 91 children with attention-deficit hyperactivity disorder, with and without comorbid tics, were determined in a 1-year prospective, placebo-controlled study at the Hospital for Sick Children, Toronto, Canada. Preexisting tics were reported in 37 (41%); 11 (24%) of 46 in the MPH group, and 16 (36%) of 45 controls. Patients previously treated for ADHD or tics and those with severe tics or Tourette's syndrome were excluded. Doses of MPH and placebo were increased weekly in 5-mg steps during an initial 3-4 week titration phase, up to a target dose of 0.7 mg/kg body weight twice daily (10-20 mg at breakfast and lunch). Doses were continually adjusted in response to behavioral changes and side effects, as observed by parents and teachers and reported by telephone, and by physician's examination at 1, 4, 8, and 12 months. The average dose of MPH was 0.5 mg/kg bid, and the target dose was not reached because of side effects. Crossover, commonly from placebo to MPH, resulted in 72 subjects in the final MPH group and only 18 of the initial 45 remaining on placebo.

Tics of varying severity developed in 20 (28%) patients receiving MPH: 12 (60%) within 4 months, 6 after 4-8 months of therapy, and 2 between 8 and 12 months. Of 9 subjects in the placebo group who developed tics, 1 (11%) occurred within 4 months, 5 from 4-8 months, and 3 between 8 and 12 months. Tourette-like syndrome developed in 2 children, both in response to MPH therapy; one had preexisting tics and the other had no prior personal history but a positive family history of tics or TS. Of 51 MPH-treated patients without prior tics, 10 (20%) developed tics, whereas in 12 receiving placebo, 2 (16%) reported tics (Fisher exact test, p=.59, not significant). (Law SF, Schachar RJ. Do typical clinical doses of methylphenidate cause tics in children treated for attention-deficit hyperactivity disorder? J Am Acad Child Adolesc Psychiatry August 1999;38:944-951). (Reprints: Dr Russell Schachar, Child Psychiatry Research Unit, The Hospital for Sick Children, 555 University Ave, Toronto, Ontario, Canada M5G 1X8).

COMMENT: The authors conclude that doses of methylphenidate (MPH), not

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exceeding 0.5 mg/kg twice daily, do not cause a significant exacerbation or precipitation of tics in children with ADHD, when evaluated over a 1-year period and relying on parent and teacher reports. However, they caution that until the effect of MPH in larger samples has been studied, using more exact measures of tics, it would be wise to monitor for tics, especially if high doses of MPH are required.

By pooling data from treatment time periods (0-4, 4-8, and 8-12 months), and by using a statistical test amenable to small numbers, the authors were unable to demonstrate a significant difference in tic prevalence among 72 MPH-treated and 18 placebo patients. The clinical significance of the study may be questioned, however: 1) the control group was relatively small; 2) the severity of tics was different in the two groups (mainly severe in MPH-treated patients and 2 with Tourette's syndrome (TS), and none severe and none with TS in the placebo group; 3) lack of agreement between teacher and parent observations (only 5 of 27 cases with tics identified by both); 4) disparity in time of onset of tics in the two groups (most MPH-related tics developed within 4 months, whereas placebo-associated tics had an onset after 4 months). In fact, if one compares the cases with tics developing within 4 months (12 (60%) of 20 in the MPH group cf to 1 (11%) of 9 placebo cases), the conclusion might be different. The long duration of the study may have influenced variables (eg. caffeine intake, streptococcal infection, environmental stress), not considered as possible aggravating factors.

The relation between MPH and tics and TS is controversial. Some authors condone neurostimulant therapy for ADHD complicated by tics or TS, but only with parental informed consent (Zametkin AJ, Ernst M. N Engl J Med 1999;340:40-46), whereas most favor avoidance of MPH in patients with a personal or family history of TS, and the use of conservative doses in treatment of ADHD (Millichap JG. Dev Med Child Neurol May 1999;41:356; Traverse L. Dev Med Child Neurol Dec 1998;40:847). Stimulant-induced tics are dose-related, a factor not addressed in the Law and Schachar, Toronto, study, occurring especially with larger doses - a 47% incidence with 0.5-1.3 mg/kg MPH (Borcherding BG et al. Psychiatry Res 1990;33:83-94; Tanner CM, Goldman SM. Neurol Clin 1997;15:395-402),

TOURETTE SYNDROME WITH GYRUS RECTUS CYSTS

Multicystic changes in the gyrus rectus of the left frontal lobe were demonstrated by brain magnetic resonance imaging in an 11-year-old boy with Tourette syndrome reported from Children's Regional Hospital at Cooper Hospital/University Medical Center, Camden, NJ. Symptoms and signs of comorbid ADHD or obsessive compulsive disorder were absent. Tics responded to low dose clonidine therapy. (McAbee GN, Wark JE, Manning A. Tourette syndrome associated with unilateral cystic changes in the gyrus rectus. Pediatr Neurol April 1999;20:322-324). (Respond: Dr McAbee, Division of Pediatric Neurology, Children's Regional Hospital, 3 Cooper Plaza, Suite 309, Camden, NJ 08103).

COMMENT. Neurobiologic studies of Tourette syndrome (TS) have previously demonstrated that the prefrontal and cingulate gyrus, midbrain, corpus callosum, limbic system, and thalamus may be involved in the pathophysiology of TS. The above case-report suggests that the gyrus rectus may also be implicated in TS, independent of the basal ganglia. (see Progress in Pediatric Neurology III, PNB Publ, 1997;pp321-323).