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ATTENTION DEFICIT AND LEARNING DISORDERS

GROWTH OF ADHD CHILDREN, STIMULANTS AND GENDER

The impact of gender, development, and stimulant therapy on the growth of children with attention-deficit/hyperactivity disorder (ADHD) was examined at the Massachusetts General Hospital (MGH), Boston. Height and weight were evaluated in 124 ADHD girls (ages 6 to 17 years) compared to 116 female controls without ADHD and in 124 boys with and 109 without ADHD. No differences were found in the age of onset of puberty in ADHD and control probands. As previously reported in an MGH study of boys with ADHD, no deficits were observed in age-adjusted height or age and height-adjusted weight in ADHD girls. Growth was not related to psychotropic treatment in the past 2 years, short stature, pubertal development, or family history of ADHD. Neither ADHD nor its treatment is associated with a significant detrimental effect on growth in height or weight. Concerns regarding putative adverse effects of stimulant therapy of ADHD on development and growth, as reported in earlier studies, should be allayed by these findings. (Biederman J, Faraone SV, Monuteaux MC et al. Growth deficits and attention-deficit/hyperactivity disorder revisited: impact of gender, development, and treatment. Pediatrics May 2003;111:1010-1016). (Reprints: J Biederman MD, Pediatric Psychopharmacology Unit (ACC 725), Massachusetts General Hospital, Fruit St, Boston, MA 02114).

COMMENT. Beginning with a report by Safer et al in the 1970s, parents voice persistent concerns about possible adverse effects of methylphenidate and other stimulants on the growth of ADHD children. Despite subsequent reports that indicate no significant association between growth and conservative treatment of ADHD (Millichap 1977, Satterfield et al 1979, Spencer et al 1996), parental concerns are exaggerated by repeated

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media attention to this problem. The excellent studies by the MGH investigators further delineate the growth of ADHD children and adolescents and emphasize the necessity to control for gender, age, pubertal development, parental height, and comorbidity in the analysis of data. Their results may need to be confirmed by additional longitudinal studies, but an emphasis on detrimental growth effects of stimulant therapy appears to be unjustified. A policy of prescribing the lowest effective dose and omitting or reducing drug treatment during weekends and holidays may be considered prudent in the management of most uncomplicated cases of ADHD.

Modified and extended-release formulations of methylphenidate and amphetamines. Once daily stimulant medications have become popular in recent years but have not entirely replaced the shorter acting preparations. The pharmacokinetics of Concerta (18mg tablet) have been compared with that of Ritalin LA (20mg capsule) in healthy adults (Markowitz JS, Straughn AB, Patrick KS et al. Clin Pharmacokinet 2003;42:393-401). The profile of Concerta rapidly reached an initial plateau concentration of 3.4 mcg/L MPH at 3.3 hours after administration and a second mean plateau concentration of 5.9 mcg/L at 6 hours. In contrast, Ritalin LA had a biphasic absorption, with a mean initial peak plasma concentration of 7 mcg/L at an average of 2.1 hours and a second peak of 9.3 mcg/L at 5.6 hours. The overall absorption of MPH was similar between the two formulations, but substantially more MPH was absorbed from Ritalin LA than from Concerta over the first 4 hours. The respective extent (area under the concentration-time curve, AUC_4) of the absorption was Ritalin LA 18.5 and Concerta 9.3 mcg h/L ($P<0.001$). Oral clearance was identical for the two formulations. The Ritalin LA appears to be about twice as potent as Concerta in the first 6 hours after administration.

The pharmacokinetics of once-daily Adderall R (10 mg) and Adderall XR (10, 20, or 30 mg) were studied in 51 children (aged 6-12 years) with ADHD. (McGough JJ, Biederman J, Greenhill LL et al. J Am Acad Child Adolesc Psychiatry June 2003;42:684-691). Substantial intersubject variability in rates and extent of absorption of Adderall XR were evidenced, underscoring the need for individual dose titration. Time to maximum concentration (Tmax) for Adderall XR versus Adderall showed average increases of 3.0 hours for dextroamphetamine and 3.2 hours for levoamphetamine. The d- and l-isomer concentrations were highly correlated, approximating a 3:1 ratio. Adderall XR showed extended Tmax values compared with Adderall and is suitable for once-daily dosing.

The safety and efficacy of Adderall XR were studied in a randomized, double-blind, crossover study of three doses (10, 20, and 30 mg), placebo, and an active control (Adderall(R) 10 mg) given once daily to 51 children with ADHD. (McCracken JT, Biederman J, Greenhill LL et al. J Am Acad Child Adolesc Psychiatry June 2003;42:673-683). Dose-dependent improvements in attention and math test performance were evident for Adderall XR. Adderall XR 20 and 30 mg and Adderall(R) 10 mg all showed improvements by 1.5 hours, but only Adderall XR 20- and 30-mg doses showed continued activity at 10.5 and 12 hours for classroom behavior and math test performance versus placebo.