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ATTENTION DEFICIT DISORDERS

SINGLE-DOSE AMPHETAMINES IN ADHD

The efficacy and time course of single morning doses of Adderall[®], extended-release (Spansules), and immediate-release (tablets) dextroamphetamine sulfate (DXA) and placebo were compared in 35 children with attention-deficit/hyperactivity disorder (ADHD) in a randomized, double-blind, crossover study at the Child Psychiatry Branch, National Institute of Mental Health, Bethesda, MD. Boys outnumbered girls, 21 to 14, and ages ranged from 6.9-12.2 years. All had severe hyperactivity, impulsivity, and inattentiveness, and 10 also had oppositional defiant disorder. Twenty had previously received stimulant therapy, usually methylphenidate. Exclusion criteria included an IQ <80, and tic, anxiety or mood disorder requiring treatment. Medications were administered for 8 weeks, each child receiving 2 weeks of each drug in random order, in doses based on age, weight, and symptom severity (means, 7.8-12.8 mg, 0.24-0.39 mg/kg). Children attended a research school 5 days a week, behavior management was used extensively, but parent training was not provided. Conners Parent and Teacher Ratings, Children's Psychiatry Ratings (Fish, 1985), academic measures at 11 am on timed math tasks, Actometer readings (Actiwatch worn on nondominant wrist), and Side Effect Ratings were collected weekly.

All 3 drugs exhibited efficacy compared to placebo. Higher doses were significantly more effective than lower doses for all medications ($p=.03$). On the Conners Teacher Hyperactivity factor score, measured in the classroom between 9 am and 12.30 pm, immediate-release DXA and Adderall decreased hyperactivity significantly more than DXA Spansules ($p=.025$). In afternoon recreation therapy (1pm-3pm), DXA Spansules decreased hyperactive behavior significantly more than Adderall ($p=.04$). DXA Spansules and tablets produced dose-related improvements whereas Adderall in increasing doses showed no dose-related improvement in the afternoons. Late afternoon parent ratings of hyperactive behavior showed significant improvements with DXA Spansules ($p=.007$) and Adderall ($p=.03$), and a trend ($p=.053$) for DXA immediate-release tablets.

On timed academic math tasks, DXA tablets and Spansules significantly increased the number and accuracy of attempts ($p=.002$ and $.003$, respectively)

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when compared to placebo. Improvements in cognition while on Adderall, at either low or high dose, did not reach significance. All 3 drugs decreased locomotor activity measurements significantly from 9am to 7pm. Activity was significantly increased from 8-9pm during treatment with immediate-release DXA. DXA Spansules were significantly more effective than both DXA tablets and Adderall between 4 and 7pm. Sleep duration was significantly decreased by DXA Spansules and tablets but not by Adderall. Nurse ratings of adverse events were increased, especially for DXA Spansules. Parent ratings of adverse events were less in the second compared to the first week of treatment. All 3 drugs significantly decreased body weight ($p < .001$), especially with higher doses of Adderall and DXA Spansules. Final review, that included parent and teacher assessments of the "best week" for each child, selected high-dose immediate-release DXA as the optimum choice for continuing open trial (in 32%), low-dose DXA Spansules (26%), high-dose Adderall (18%), high-dose DXA Spansules (12%), and low-dose Adderall and low-dose DXA tablets, both (6%). Seventeen received a brief open trial of methylphenidate (MPH) at the conclusion of the study, as an option for further treatment. At discharge, 12 (34%) were placed on immediate-release DXA, 8 (23%) on MPH, 6 (17%) on Adderall, and 5 (14%) on DXA Spansules. (James RS, Sharp WS, Bastain TM et al. Double-blind, placebo-controlled study of single-dose amphetamine formulations in ADHD. J Am Acad Child Adolesc Psychiatry November 2001;40:1268-1276). (Reprints: F Xavier Castellanos MD, NYU Child Study Center, 577 First Ave, New York, NY 10016).

COMMENT. This is the first controlled comparison of Adderall and both DXA tablets and Spansules. Whereas the control of hyperactive behavior by Adderall began earlier than the response to both DXA preparations and continued up to 13 hours after a single morning dose, DXA Spansules were superior to Adderall in decreasing hyperactivity in early afternoon and evening. Spansules exhibited significant and better effects than Adderall on academic performance. Immediate-release DXA was chosen most frequently by parents, teachers and staff as the overall optimum therapy for ADHD. Future studies may show that multiple doses or a combination of immediate-release DXA and Spansules are superior to single doses of either drug alone in some patients. With the recent mushrooming introduction of alternative, sustained release stimulants (Concerta, Adderall ER, etc) for the treatment of ADHD, well controlled studies similar to the above will be needed to demonstrate their superiority to existing less costly preparations. Extended release medications avoid school nurse administration when an all day effect is desired, but adverse events may be increased.

Methylphenidate enhances task-switching performance in a study of 20 children with ADHD at the University of Illinois at Urbana-Champaign, IL (Kramer AF, Cepeda NJ, Cepeda ML. J Am Acad Child Adolesc Psychiatry Nov 2001;40:1277-1264). MPH selectively facilitates inhibitory cognitive processes which allow performance and coordination of multiple tasks.

TIC DISORDER AND ADHD

The behavioral and neuropsychological characteristics of tic disorder, with or without attention-deficit hyperactivity disorder (ADHD), were examined in 78 children followed at Seoul National University College of Medicine, Korea. Sixteen had tic disorder alone, 19 had comorbid tics and ADHD, 21 had ADHD alone, and 22 were normal controls. Seven neuropsychological tests involving global cognitive function, attention, information-processing, and fine motor coordination were compared in the 4 groups. Tic disorder with ADHD and ADHD patients had similar