Managing Growth Deceleration Associated With Attention-Deficit/Hyperactivity Disorder and Stimulant-Induced Appetite Suppression

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Central nervous system stimulants are prescribed to children and adolescents with increasing frequency for treatment of attention-deficit/hyperactivity disorder (ADHD).[1] Due to their well-established safety profile and high efficacy, stimulants are used first line to support learning and interpersonal functioning in children with ADHD. Caution must still be used when prescribing stimulants, which are associated with appetite suppression and weight loss in children. Since the benefits of stimulants were first established, concern has grown for stimulant-associated growth deceleration and persisting limits on adult height.

The Multimodal Treatment of Attention-Deficit Hyperactivity Disorder Study (MTA), sponsored by the National Institute of Mental Health in 1997, focused on the comparative efficacy between stimulant medication, behavior therapy, a combination of both, and usual community care.[2] At the time the MTA was first conducted, there was little concern that use of stimulants for ADHD would meaningfully affect children's size. However, more recent research on stimulant use in children has demonstrated height and weight deceleration without evidence of growth rebound.[2-4]

A 36-month follow-up study conducted to address some of the MTA's limitations found that newly medicated children who initiated stimulants during the surveillance period grew an average of 2.0 cm and 2.7 kg less than the children who remained unmedicated.[2] A 16-year MTA follow-up study showed that consistently medicated participants (used ≥50% of days during every measured time interval) had a significantly shorter sex-corrected height (4.7cm/1.9 inches, $P<0.001$) than participants with ADHD who had negligible exposure to stimulants.[3]

Stimulant-induced appetite suppression may contribute to slowing of growth.[4] Accordingly, increasing caloric intake may help to offset the decrease in weight gain in children taking stimulants. In 2020, a randomized controlled trial involving 230 children ages 5-12 with no history of chronic stimulant use examined the efficacy of weight recovery treatments (WRTs).[5] Children were randomly assigned either to treatment with daily methylphenidate or to behavior therapy.[5] The children who showed a decrease in BMI of > 0.5 z-units after 6 months of methylphenidate were randomly assigned to 1 of 3 WRT groups: monthly monitoring of height and weight, drug holidays (medicating for school hours only), and 150 kcal/day caloric supplementation.[5] Although children assigned to all 3 WRT groups increased their weight velocity, recovery was greater for those who took drug holidays or caloric supplements.[5] None of the WRTs were associated with an increase in height velocity.[5]

If tolerated, a child with significant appetite suppression may recover some weight by medicating only during school hours with a shorter-acting stimulant and not taking medication on days without school.[5] However, shorter-acting formulations have the disadvantage of waning therapeutic effect later in the day.[6] Worsening ADHD symptoms during nonmedicated hours may make it necessary to try different weight recovery methods. To maximize caloric intake, it is important to know how the patient is taking stimulant medication in relation to mealtimes.

When a child presents with reduced appetite and/or diminished growth, a range of potential causes must be investigated. Even when stimulant medication is the likely culprit, the benefits of stimulant medication

for a particular child's overall functioning may justify continuing the medication and addressing appetite suppression by other means.

We suggest the following measures when a patient taking stimulants for ADHD presents with decreased appetite and/or growth:

Thorough Medical and Psychiatric History Including Screening For Substance Abuse

Medical conditions unrelated to prescription stimulant use may contribute to decreased appetite and weight loss. Decreased oral intake may be a presenting symptom in diabetes, hypothyroidism, inflammatory bowel disease, malignancy, and a variety of other causes.[7] Substance abuse history is important, especially with methamphetamine, cocaine, or other non-prescribed stimulants, and potentially can cause further appetite suppression and weight loss.[8] Loss of appetite may also be a symptom of depression, anxiety, or eating disorders.[7] Patient T, a 16-year-old female treated for ADHD at our child psychiatry clinic, was taking both amphetamine-dextroamphetamine and sertraline 25 mg daily when she presented with depressed mood. Patient T's symptoms included low energy, lack of interest, lack of motivation, poor appetite and weight loss. After her sertraline was gradually increased to 100 mg daily, her appetite improved, and weight loss resolved within the next several months.

Complete and Accurate List of Prescribed and Nonprescribed Medications

Other medications and supplements with appetite-suppressing effects may be taken concurrently with stimulant medication. For example, decreased appetite is associated with use of bupropion, topiramate, amantadine, spironolactone, nitrofurantoin, itraconazole, and hydroxyurea.[9] In the case of patient X, a 15-year-old male with poor appetite and BMI of 16.6 treated for ADHD, improved appetite and weight gain were achieved by managing medications without discontinuing the stimulant. Upon inquiry it was discovered that in addition to methylphenidate extended release 18 mg daily, Patient X was also taking topiramate 100 mg daily as prescribed by his neurologist for treatment of his tic disorder. When tics were under control, topiramate was tapered and discontinued by his neurologist. His appetite and weight had increased when he followed up with psychiatry after discontinuation of topiramate.

Drug Holidays and Caloric Supplementation

As demonstrated by Waxmonsky *et al.* in the trial of weight recovery treatments (WRTs) for stimulant-associated growth restriction, increasing caloric intake by use of supplements and strategic timing of medications may help to restore weight velocity.[5] Parents or caregivers may be encouraged to maximize the child's caloric intake by offering food when appetite is highest. Administering medication with or after a full meal may allow for sufficient nutrient intake before the medication begins to have appetite-suppressing effects. Patient Y, a 14-year-old male, responded well to methylphenidate extended-release 54 mg daily for ADHD but had reduced appetite with lack of weight gain. It was then discovered that Patient Y was taking methylphenidate on an empty stomach in the morning at least one hour before breakfast. His weight increased after he began taking methylphenidate with a full breakfast. Other helpful strategies for increasing caloric intake include offering a small bedtime snack or delaying dinnertime until after stimulant medication effects wear off.

For children who can tolerate drug holidays on non-school days, nutrient intake on weekends may help to offset poor appetite on school days. Patient Z, a 9-year-old male treated with methylphenidate, was not gaining weight as expected for a child his age. Patient Z had gained weight at his 2-month follow-up after his parents stopped administering methylphenidate on weekends and holidays.

Regular Monitoring of Height and Weight

Although the effect was smaller in the monitoring group than the drug holiday or caloric supplementation groups, Waxmonsky *et al.* found that in children whose BMI decreased with initiation of stimulants, measuring weight and height on a monthly basis increased weight

velocity.[5] In theory, regular monitoring may be helpful because it keeps parents and caregivers mindful of any changes in growth.[5] This awareness may lead caregivers to limit medication frequency and increase the child's caloric intake.

Treatment of ADHD in children and adolescents must be individualized. If stimulant medication improves decision-making and learning ability for a child with ADHD, these benefits must be considered along with the stimulant's potentially negative effects on physical growth. If lack of growth is significant or does not respond to the above recommendations, the clinician may consider a different type of stimulant or a trial of non-stimulant medication. This approach may help to optimally treat ADHD symptoms while keeping appetite and growth effects manageable.

Take Home Summary

Growth deceleration in height and weight has been associated with stimulant medication use in children with ADHD. These effects may persist into adulthood. We propose methods for growth rate management in children who benefit from stimulants for learning and interpersonal functioning.

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