Pharmacological Management of Preschool ADHD

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PRESCHOOL ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) VIGNETTE

A 4½-year-old girl with ADHD, combined subtype, and oppositional defiant disorder presents for evaluation and initiation of treatment. She has severe symptoms of inattention, hyperactivity, and impulsivity, leading to significant impairment in multiple domains. Peer relationships are strained, and she was admitted to the emergency department twice last year (once after darting in front of a car and once when she tipped her chair over backward in class). The child was recently expelled from her second preschool this year because of disruptive and out-of-control behavior. The parents received training in behavior modification (parent training), but despite their close adherence, little improvement in the child’s behavior was noted.

HOW WOULD YOU ADDRESS THIS PHARMACOLOGICALLY?

Helen Egger, M.D.

As with older children, the assessment of preschool children must be comprehensive, accounting both for psychiatric and medical comorbidity and for co-occurrence of developmental delays in language, cognitive, learning, and motor domains. It is important to take a careful history of the family structure, current parental psychiatric illness and substance use/abuse, parental stress, and the child’s history of stressful life events. The child’s environment must also be carefully assessed, including evaluation of the quality of the child’s relationship with her primary caregivers through both parent report and observation. A comprehensive assessment of a preschooler must be based on information gathered from multiple informants including parents, teachers/daycare providers, other important caregivers such as a grandparent or nanny, other medical providers such as a pediatrician, and the child. It is not sufficient to gather information only from adults. The clinician must assess the child directly, interacting with the child in both structured (e.g., testing) and unstructured or semistructured ways. The child and adolescent psychiatrist should then ensure that the information from these assessments is integrated into a comprehensive treatment plan.

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We are told that this girl meets criteria for ADHD and oppositional defiant disorder, and certainly the details provided point to these diagnoses. It is critical to rule out an anxiety disorder, particularly separation anxiety disorder or PTSD, depression, or a pervasive developmental disorder, which commonly present in...
young children with severe irritability including temper tantrums, disruptive behavior, oppositionality, and inattention.

Because there are so few data on the treatment of preschoolers, I recommend a structured, empirically based approach to determining whether the treatment, psychosocial or pharmacological, is effective. In light of the lack of treatment studies, as well as the potential risks of treatment, in our clinic, we use a single-case experimental design in planning, implementing, and determining the effectiveness of treatment in young children. Published guidelines are available on the design, implementation, and interpretation of single-case experimental designs (Hayes et al., 1999, Sackett et al., 2000).

A cornerstone of this approach is the identification of clearly defined target symptoms, ideally using developmentally appropriate, reliable, and valid measures that are sensitive to change, so that the clinician will be able to assess the effectiveness of the intervention and the outcome of treatment. Handbook of Infant, Toddler, and Preschool Mental Health Assessment is an excellent resource about measures to be used to assess preschool mental health symptoms and disorders (DelCarmen-Wiggins and Carter, 2004). Carter and colleagues (2004) also provides a useful overview of measures.

In this vignette, the psychiatrist and the parents have tried parent training with no significant change in the child’s symptoms or improvement in her functioning. Assuming the domains such as language or parental psychopathology or stress are also being addressed, it seems appropriate to initiate a trial of stimulants, using parent and teacher measures such as the Conners Parent Rating Scale-Revised and the Conners Teacher Rating Scale-Revised (validatated for children 3 years old and older) (Conners et al., 1998) to identify baseline ADHD symptoms and track response to treatment. Scales should be completed weekly during the initial treatment period. I would start with a trial of a short-acting stimulant on a weekend to determine responsivity and tolerance before switching to a long-acting stimulant. It is important to track the child’s height and weight and recommend high-protein, high-energy (calorie) bedtime snacks if the child is experiencing significant appetite reduction on the medication. Although medication can be mixed with pudding or jam, we have been successful teaching young children to swallow pills using this mini-M&M technique: the child holds a gulp of water in her mouth, drops a mini-M&M in the “pool,” and then swallows.

I would not recommend the use of typical or atypical antipsychotics for this child or for most other young children, except perhaps with great caution for those children who are so severely aggressive that they pose a risk of significant harm to themselves or other children. I would also strongly advise against the use of multiple medications. Last, if the child responds to the medication, then we would expect to see decreased impairment in the child and decreased family disruption and distress. It may be appropriate at this point to try parent training again to see whether there may now be a more fertile ground for these valuable skills to be useful.

Laurence L. Greenhill, M.D.

The vignette presented is of a 4½-year-old girl with ADHD, combined subtype, and with oppositional defiant disorder that has been associated with significant impairment across several domains: poor peer relationships, repeated physical injury, and expulsion from two preschool programs. She has been referred for evaluation and treatment.

I would recommend that this child be referred to a child psychiatrist for evaluation and treatment. The assessment should include a complete developmental history, family history of disruptive behavior disorders in other family members, and questions about possible physical and sexual abuse. Current opinion among child psychiatrists suggests that impairing symptoms of ADHD must be present in more than one setting. I would want to collect information on the impairment from parents but also from the teachers, day care providers, primary care clinicians, as well as the child. In our clinic, we use a rating scale such as the Conners rating scales, including the Conners Parent Rating Scale-Revised, and Conner Teacher Rating Scale-Revised, which have norms for children as young as 3 years of age, gathered before a treatment intervention. The duration of the disruptive behaviors needs to be chronicled because those with stable ADHD will most likely have symptoms lasting more than 9 months. A careful review of symptoms needs to be taken to rule out other disorders, such as anxiety disorders, depressive disorders, bipolar disorder, or pervasive developmental disorders that may better explain the child’s symptoms and
impairment than ADHD does. A physical examination should be done to assess for evidence of abuse.

The treatment history, both psychosocial and pharmacological, should be reviewed. For those families previously exposed to parent training, information on the number of sessions, duration of each session, attendance rates by the parents, and homework completion needs to be gathered. One must establish that the parents were compliant, did the homework, and were judged by the trainer as having reached a good level of understanding of the principles of behavioral modification.

The parents should be interviewed to get a thorough understanding of their attitudes toward all forms of intervention, including behavioral modification, special schooling, further parent training, and psychopharmacological intervention. I would inquire specifically about attitudes regarding stimulant medications. If the parents are willing for their daughter to be treated, then it would be wise to select an end point in terms of the child’s current impairment. For this child, the elimination of disruptive behaviors in the classroom, reduced observed motor activity, and decrease in impulsivity in the home can be used as barometers of response.

At this time, the FDA lists only d-amphetamine (Dexedrine) as approved for treatment of a child between the ages of 3 and 6 years. Because more data are available regarding the use of methylphenidate in this population, methylphenidate would be my first choice of the stimulant medications. Data from the double-blind, placebo-controlled, crossover titration trial in the Preschool ADHD Treatment Study (PATS) suggest that preschool children need to be started on low doses of stimulant medication (Greenhill et al., in press). For example, I would start this child on the lowest dose of a long-duration beaded methylphenidate, such as half of the beads from a 10-mg capsule of Ritalin LA, given once in the morning. I would schedule a visit for the child and family to return to the clinic after 1 week on this dose, during the period of time the medication is active, between 9 A.M. and 3 P.M. Direct observation, information from parents on impulsive behavior, and information from the teacher about disruptive behaviors should be collected. As indicated and tolerated, I would gradually increase the total daily dose to a maximum of 30 mg. (The mean optimal dose in the PATS double-blind, placebo-controlled dose-ranging trial was 14 mg of methylphenidate total daily dose.) Other options that use the beaded methylphenidate delivery system include Focalin XR or Metadate CD. Concerta is a potential option for those youngsters who are able to swallow capsules.

Although I would recommend starting with a methylphenidate product, d-amphetamine is approved for children with ADHD as young as age 3, so this would be my second-line choice. I would start with 2.5 mg d-amphetamine (half of a 5-mg tablet), given after breakfast and after lunch. If the child continues to be impulsive at home and disruptive at school, then this dose can be increased to 5 mg at 8 A.M. after breakfast, and 2.5 mg at lunch for the next week. Again, the family should come in and the events of the past week reviewed. If the desired symptom end points have not been reached, then an increase to 5 mg twice daily could be given. The child can continue this titration, as indicated, up to a daily d-amphetamine dose of 10 mg b.i.d.

If the predetermined criteria for response are reached, then I would consider switching the child to d-amphetamine spansules if the child can swallow the capsules whole, or to Adderall XR if the child needs the amphetamine sprinkled on her food to swallow the medication.

If the child does not respond satisfactorily to methylphenidate or amphetamine or side effects intrude, then I may shift the treatment to atomoxetine as a third level of treatment. No data have been published for children under age 6, however. It is this clinician’s impression that the weight-adjusted doses for atomoxetine work as satisfactorily with preschoolers as they do with school-age children.

James J. McGough, M.D.

Given the inadequate evidence base supporting medication treatment of ADHD in preschool-age children, initiation of pharmacotherapy in this patient requires careful consideration of possible benefits versus risks. Risk assessment is complicated by our complete lack of understanding of the long-term consequences on brain development and general health of giving psychotropic medications to young children. Preclinical studies with juvenile rats suggest that early exposure to methylphenidate induces early gene activation consistent with long-term brain reorganization (Brandon and Steiner, 2003) and may increase risk of anxiety in adulthood (Bolanos et al., 2003). In this particular case, however, the child clearly has unacceptable risks for long-term difficulties in home, school, and peer functioning. Medication treatment is clearly acceptable...
in view of the failure of psychosocial interventions to provide sufficient behavioral control.

Dextroamphetamine has FDA approval for ADHD treatment in children as young as 3 years, and methylphenidate carries an FDA warning that it not be used in children younger than 6 years old. Neither the approval nor the warning is based on data. Nonetheless, methylphenidate is the most commonly used psychotropic agent in preschool-age children. Its use in this age group has increased dramatically during the past decade (Zito et al., 2000). The short-term efficacy and tolerability of immediate-release methylphenidate for preschool ADHD was recently demonstrated in the large, National Institute on Mental Health–funded, multisite PATS (Greenhill et al., in press). I am not aware of any published studies of nonstimulant medication for preschool ADHD. Medication selection for the present case should be based on known efficacy data, anticipated side effects, and ease of use.

Because of concerns about appetite loss and possible growth suppression, I would prefer to use a form of methylphenidate in younger children instead of amphetamine, which is more potent and often more likely to cause anorexia. Consistent with current practice, I would also favor a formulation suitable for once-daily dosing to decrease risks of social stigma and improve compliance. Unfortunately, the most frequently prescribed formulation, OROS-methylphenidate, is available only in large capsules, which may be difficult for younger patients to swallow. Beaded preparations, which can be removed from their capsules and sprinkled on food, are more suitable for preschoolers. Based on results from PATS, which found a mean optimal daily dose of 14 mg, I would begin titration with a 10-mg beaded, extended-release methylphenidate for 1 week, then increase by 10 mg/week for 2 additional weeks. Alternatively, one could begin with a 5-mg dose of the recently FDA–approved beaded formulation of extended-release dexamphetamine and subsequently increase this dose in 5-mg increments. Premedication baseline and weekly ratings of ADHD symptoms should be obtained from parents and teachers (when available) using a standard DSM-IV-based ADHD rating scale. ADHD response and side effects should be monitored at weekly visits. Height and weight should be measured at baseline and observed during treatment. After reviewing all of the information from the titration, I would choose a “best dose” that optimizes ADHD improvement with minimal side effects. If the methylphenidate trial was unsuccessful, then I would repeat a similar titration beginning with a 5-mg extended-release amphetamine, such as mixed amphetamine salts, which also uses a beaded delivery system suitable for sprinkling on food. Once available, patch formulations of methylphenidate, currently in development, are likely to be an excellent choice for treating preschool children. I would reevaluate the child off medication every 6 to 12 months to ensure ongoing need and monitor weight and height during the course of therapy for comparison with expected development.

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REFERENCES