Drug Treatment for Hyperactive Children
Therapeutic Guidelines

Josephine Elia
The Medical College of Pennsylvania, Philadelphia, Pennsylvania, USA

Contents

Summary
1. Pharmacotherapeutic Agents
   1.1 Central Stimulants
   1.2 Antidepressants
   1.3 Other Agents

2. Diverse ADHD Populations
   2.1 Girls
   2.2 Comorbid Disorders
   2.3 Tourette’s Disorder

3. Conclusions

Summary
Attention deficit hyperactivity disorder (ADHD) is a common childhood behavioural disorder and medication is one of the principal treatments. Methylphenidate and dexamphetamine (dextroamphetamine) have a long record of use in children and well proven efficacy, and are the preferred drugs. Current clinical guidelines recommend a trial of methylphenidate and of dextroamphetamine for each child meeting criteria for the disorder in order to maximise response rate and minimise adverse effects.

Attention deficit hyperactivity disorder (ADHD) is a complex, heterogeneous disorder manifested by varying degrees of developmentally inappropriate hyperactivity, distractibility and impulsiveness. It occurs in approximately 1 to 4% of children, with a higher prevalence in boys than girls (Szatmari et al. 1989). The Diagnostic and Statistical Manual of Mental Disorders, 3rd edition, revised (DSM-III-R) diagnostic criteria requires the presence for ≥6 months of ≥8 of the symptoms listed in table I.

Typically beginning in childhood, symptoms may become manifest at home, school or social settings, frequently leading to academic and social impairments. Symptoms are exacerbated in group settings or distractible situations and are decreased in highly structured and supervised settings.

Medication is the principal therapy for children with ADHD, and dexamphetamine (dextroamphetamine) and methylphenidate should be the first choice in treatment. However, given the complexity of this disorder, associated comorbid disorders, as well as the wide-ranging effects of the behavioural problems, multimodal treatments are frequently necessary. The degree of impairment can be used
Table I. Diagnostic and Statistical Manual of Mental Disorders, 3rd edition, revised (DSM-III-R) criteria for ADHD (American Psychiatric Association 1987)

Child has ≥8 of the following symptoms for ≥6 months:
1. Often fidgets with hands or feet or squirms in seat
2. Has difficulty remaining seated when required to do so
3. Is easily distracted by external stimuli
4. Has difficulty waiting in turn in games or other group situations
5. Often shouts out answers to questions before they have been completed
6. Has difficulty following through on instructions from others
7. Has difficulty sustaining attention in tasks or play activities
8. Often shifts from one uncompleted activity to another
9. Has difficulty playing quietly
10. Often talks excessively
11. Often interrupts or intrudes on others
12. Often does not seem to listen to what is being said to him/her
13. Often loses things necessary for tasks or activities
14. Often engages in physically dangerous activities without considering possible consequences

as a guideline in determining treatment. Children with minimal impairment may need medication or a highly structured setting, while children with moderate to severe impairment frequently need medication in addition to other treatment modalities, which can include behaviour modification, patient and parent counselling and school-based behavioural interventions.

Diagnosis of ADHD is currently reached through a thorough clinical evaluation. There are no brain-imaging techniques or diagnostic tests to confirm it. Response to the stimulant medications is likewise not diagnostic since the same effects have been found to result in normal children (Rapoport et al. 1978, 1980).

1. Pharmaco-therapeutic Agents
1.1 Central Stimulants

The mechanism of action of central stimulants in children with ADHD is unclear. Both dexamphetamine and methylphenidate block the reuptake of dopamine and noradrenaline (norepinephrine) [Kuczenski 1983]. Biochemical studies exploring urinary and plasma levels of these neurotransmitters and their metabolites in ADHD children, however, have been inconclusive. Levels of homovanillic acid, the major metabolite of dopamine, were unaffected by either drug, while urinary noradrenaline and its metabolite 3-methoxy-4-hydroxyphenylglycol were decreased by dexamphetamine, and unchanged by methylphenidate (Elia et al. 1990).

1.1.1 Dexamphetamine

Amphetamines were the first group of medications found to be effective in controlling behavioural disorders in children (Bradley 1937). Dexamphetamine is currently preferred over the racemic or levodopa formulae due to its quicker onset of action and greater efficacy (Stimmel 1989). It is completely absorbed following oral administration, achieving a peak concentration in 2 to 3 hours. Clinical onset of action occurs within 15 to 30 minutes and efficacy persists for 2 to 6 hours (Stimmel 1989), half-life being 4 to 6 hours (Angrist et al. 1987; Brown et al. 1979). The wide range is a result of interindividual variability.

Therapy is usually initiated with a 5mg tablet given in the morning with breakfast to minimise the risk of an upset stomach. The dosage can be increased by 5mg every 3 to 5 days in order to allow adequate time for clinicians, parents and teachers to assess response and monitor adverse effects. Once an effective dosage and the length of time that the medication is effective are established for an individual child, a second daily dose may be started if necessary. This second dose frequently can be 5 to 10mg less than the initial dose because of the long half-life of the drug. For children with severe symptoms and in whom the duration of action of the drug is brief, a third daily dose may be considered if adverse effects are tolerable. The maximal total daily dose should be 1.5 mg/kg/day.

1.1.2 Methylphenidate

Methylphenidate is a piperidine derivative structurally related to amphetamine. It is well ab-