Management of ADHD in children and adolescents

JACKIE PICKETT

Attention deficit hyperactivity disorder (ADHD) is a condition characterised by inattention, hyperactivity and impulsivity that is often diagnosed in early childhood and can interfere with school life and social functioning. This article discusses the assessment of children and adolescents with suspected ADHD, common co-morbidities and the properties of the drug treatment options available.

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental condition that presents with persistent and impairing symptoms of hyperactivity, impulsivity and/or inattention. It is caused by both genetic and environmental factors. A 2010 study found worldwide point prevalence rates of 2.2 per cent in males and 0.7 per cent in females[1] although only around 0.7 per cent of school aged children are identified clinically in the UK.[2,3]

For a diagnosis of ADHD to be made, symptoms of hyperactivity, impulsivity and/or inattention have to meet DSM-5 diagnostic criteria,[4] be associated with at least moderate psychological, social and/or educational impairment and be pervasive, occurring in two or more settings including social, familial and/or educational settings. The ICD-10[5] diagnosis of hyperkinetic disorder has narrower criteria and defines a subgroup with a more severe form of ADHD (see Table 1).

DSM-5: Six or more symptoms from either or both categories are required for a diagnosis

Inattention
- Makes careless mistakes
- Has difficulty sustaining attention in tasks or play activities
- Does not seem to listen when spoken to directly
- Does not follow through on instructions and fails to finish homework
- Has trouble organising tasks and activities
- Avoids tasks that require sustained mental effort
- Loses things necessary for tasks or activities
- Easily distracted
- Forgetful

Hyperactivity and impulsivity
- Fidgets with hands or feet and squirms in seat
- Leaves seat in situations where remaining seated is expected
- Runs about or climbs excessively in situations where these are inappropriate
- Has difficulty playing or engaging in activities quietly
- Talks excessively
- "On the go" or often acts as if "driven by a motor"
- Has difficulty waiting turn
- Blurts out answers before a question has been completed
- Interrupts or intrudes on others

Symptoms are:
- Present for at least six months
- Presenting before age 12 years (if ≥17 years, only five symptoms in each category are required for a diagnosis)
- Present in at least two settings and symptoms interfere with quality of school or social functioning
- Maladaptive and inconsistent with developmental level
- Cannot be better explained by another mental disorder

ICD-10 diagnostic criteria: differences from DSM-5

- Requires symptoms across both inattentive and hyperactive/impulsive domains
- Onset before the age of six years
- Requires direct observation of inattention/hyperactivity by clinician

Table 1. DSM-5 and ICD-10 diagnostic criteria for ADHD[4,5]

Overactivity, impulsivity, poor concentration and disruptive behaviour are often first noted in the preschool period by parents or nursery staff and brought to the attention of primary care. At this point, a period of "watchful waiting" and referral to group behavioural parent train-

ing, *eg* Triple P (http://www.triplep.net), Incredible Years (incredibleyears.com), Mellow Parenting (www.mellowparenting.org), are indicated, without the need for a diagnosis. If group participation is not possible or the family's needs are complex then individual parent training can be considered.[6,7]

If difficulties persist then a referral should be made to secondary care, either to a paediatrician with expertise in ADHD, a child and adolescent psychiatrist or a Child and Adolescent Mental Health Services (CAMHS) ADHD team.[6]

Assessment

A comprehensive assessment is required to identify ADHD and any co-morbidities or alternative diagnoses. ADHD is commonly co-morbid with other disorders (including autism spectrum disorder (ASD), tic disorders, emotional disorders, oppositional defiant disorder (ODD) and conduct disorder, substance misuse, specific learning disorders and developmental co-ordination disorders) and one of the challenges in assessment can be weighing up the relative contribution of each disorder to the child's difficulties and the priorities for intervention.

Assessment would usually comprise an account of the current difficulties, a detailed developmental history (including obstetric and perinatal complications), past medical history, family history, information about the child's functioning across a range of settings (home, school, nursery), information about educational attainment and an individual interview with the child. Observation of the child in school or nursery and completion of rating scales, *eg* Conners,[8] Strengths and Difficulties Questionnaire (SDQ),[9] can add useful information. Ideally there should be a multidisciplinary review of the information and diagnosis made by a clinician with training and expertise in the diagnosis of ADHD.[6]

Along with feedback about the diagnosis of ADHD, written information should be provided,[6] and strategies for intervention and the potential risks and benefits of these discussed. There should also be feedback to the referrer, school, educational psychologist and any other agencies involved.[6,7]

Liaison with educational establishments on an ongoing basis is particularly important, to monitor the impact of any treatment interventions. Educational psychologists can advise on classroom behaviour management strategies. Contingency management strategies and academic interventions have been shown to be more effective for behaviour change than cognitive behavioural therapy (CBT).[7] Local multiagency integrated care pathways are helpful in guiding onward referral and appropriate intervention and liaison between agencies.[6,7]

Management

When selecting the most effective intervention for symptom management in school aged children with ADHD, the severity of ADHD symptoms, the presence of co-morbidities and the socioeconomic circumstances should be considered.

Current NICE guidance is that behavioural parent training should be offered in the first instance for mild/moderate ADHD and if the symptoms do not respond, then medication should be offered. The evidence for the impact of behavioural parent training on core ADHD symptoms is limited;[10] however, preadolescent children with co-morbid generalised anxiety disorders or co-morbid ODD and/or aggressive behaviour may benefit from a combination of medication and behavioural treatments.[7] For severe ADHD/hyperkinetic disorder, medication is the treatment of choice.[6,7,11]

Drug treatment

All medications for ADHD aim to improve the core symptoms of overactivity, inattention and impulsivity. Drug treatment should be initiated in secondary care by a suitably qualified professional with expertise in the management of ADHD.[6,7]

The psychostimulants methylphenidate and dexamfetamine (including the newer long-acting prodrug lisdexamfetamine) and the selective noradrenaline reuptake inhibitor atomoxetine are the drugs currently approved in the UK for treatment of ADHD in children and adolescents. All have been shown to improve the core symptoms of ADHD and improve quality of life, with an effect size of about 1.0 for the psychostimulants and 0.7 for atomoxetine.[12]

Psychostimulants

Stimulant medications (methylphenidate and dexamfetamine) are the psychopharmacological treatment of choice for ADHD. Both are controlled drugs. They increase centrally available dopamine and noradrenaline by blocking reuptake and, in the case of dexamfetamine, also releasing dopamine stored in presynaptic vesicles. Up to 85 per cent of patients respond to psychostimulants if both methylphenidate and dexamfetamine are tried, with about 40 per cent responding equally well to both and about 45 per cent responding preferentially to one or the other.[12]

Prior to starting medication, a full past medical history should be taken, including assessment of any history of exercise syncope, undue breathlessness or other cardiovascular symptoms. An ECG is indicated if there is a past medical or family history of serious cardiac disease, a history of sudden death in young family members or abnormal findings on cardiovascular examination. Some guidance suggests that psychostimulants should not be first-line medication for children with ADHD where there are known (or where there is a family history of) cardiac abnormalities;[7] discussion with a cardiologist may help to weigh up the relative risks and benefits in proceeding with a trial of psychostimulant medication.

Baseline height, weight, blood pressure and pulse should be measured prior to initiation of medication, then following any change in dose and thereafter at three- to six-monthly intervals. Measurements should be plotted on growth and centile charts in order to monitor growth trajectories and any changes in pulse and blood pressure.[6,7]

Mild side-effects such as headache, nausea, abdominal pain and emotional lability are common on initiation of medication but tend to resolve over the first week or so. Reduction in appetite, potentially leading to a reduction in rate of growth in height and weight, and sleep difficulties more often persist. Slight increases in blood pressure and heart

rate are also common. There is debate about the association of tics with stimulant use.[7] Tics may appear to worsen or present for the first time with medication but the natural history of tics is to wax and wane and ADHD is not uncommonly co-morbid with tic disorders. Current advice would be to continue with psychostimulants and monitor tic activity, but if this persists or is problematic then a change to a nonstimulant preparation should be considered.

Choice of preparation

Over the last 10–15 years, an increasing range of modified-release preparations of methylphenidate has become available, as well as the long-acting prodrug lisdexamfetamine within the last three years.

There are preparations with differing mechanisms of delivery, differing release profiles and duration of action available (see Table 2), ranging from immediate-release methylphenidate or dexamfetamine (duration of action three to four hours) to lisdexamfetamine (duration of action 13 hours) although all are equally effective.[13]

Modified-release preparations offer a number of potential benefits – convenience, improved adherence, reduction of stigma in school (as the child does not need to take medication in school hours) and fewer problems for schools in storing and administering controlled drugs. Immediate-release preparations are useful where more flexible dosing regimens are required and in initial titration to determine the most effective dosing levels.[6]

Following a discussion with the child/young person and their family, the choice of psychostimulant should be based on the length of cover required, whether there will be problems with taking medication in school, the risk of misuse (modified-release preparations having less abuse potential), how easy it is to swallow (children with ASD and sensory issues can struggle with tablets), the side-effect profile, co-morbid disorders and cost. Lisdexamfetamine and dexamfetamine are at present licensed in the UK only for use if there is a clinically inadequate response to methylphenidate; this may relate in part to appraisal of dexamfetamine as a drug with a greater abuse potential,[14] although lisdexamfetamine itself has little potential for abuse.

Stimulant medication should be titrated to an optimal dose over a period of four to six weeks, with close contact being maintained with the child and family to monitor side-effects. Methylphenidate can be increased up to the maximum 60mg daily *BNF* limit for children and adolescents. For dexamfetamine the initial dose recommended is 5–10mg daily up to 20mg daily, depending on body weight. The maximum dosage for children and young people is 40mg daily. Lisdexamfetamine can be initiated at 30mg daily with increases of 20mg at weekly intervals up to a maximum of 70mg daily.

Name	Approximate duration of action	Formulation	Release profile (methylphenidate only)	Administration details
Immediate-release methylphenidate	4 hours	Tablet	100% immediate release	Tablets can be halved
Equasym XL (methylphenidate)	8 hours	Capsule	30% immediate release, 70% modified release	Can be opened and sprinkled over soft food then swallowed without chewing
Medikinet XL (methylphenidate)	8 hours	Capsule	50% immediate release, 50% modified release	Can be opened and sprinkled over soft food then swallowed without chewing Ingestion with high fat content food delays absorption by approx 1.5 hours
Concerta XL (methylphenidate)	12 hours	Casule-shaped tablet	22% immediate release, 78% modified release	Tablet must be swallowed whole
Dexamfetamine	4 hours	Tablet		
Lisdexamfetamine (Elvanse)	13 hours	Capsule		Can be dissolved in water
Atomoxetine (Strattera)	24 hours	Capsule or liquid		

Table 2. Properties of drugs used in the treatment of ADHD

Atomoxetine

Atomoxetine is a selective noradrenaline reuptake inhibitor. It does not lead to significant increases in dopamine levels and this means that it has less potential to become addictive than stimulant medication. Typically it does not complicate or cause tic disorders. It may therefore be more suitable for use where there is the potential for drug misuse or where tics have persisted or worsened on stimulant medication. It provides up to 24 hours of coverage (although it is possibly more effective for the first 12 hours) and this may be of benefit compared to stimulants when ADHD-related symptoms cause difficulty in the mornings prior to administration/onset of action of medication and in the evenings after medication has worn off. Unlike the stimulants, atomoxetine is not a controlled drug and some parents

prefer it for this reason. Unlike the immediate impact of stimulants, atomoxetine takes four to six weeks to begin to have an effect, and patients and families need to be made aware of this.

Common side-effects include abdominal pain, decreased appetite, nausea and vomiting, early morning wakening, irritability and mood swings, increased heart rate and small increases in blood pressure. There is a reported slight increase in suicidal thoughts on starting atomoxetine and therefore mood should be monitored carefully during the initial treatment period. A rare and idiosyncratic but mostly reversible side-effect of liver damage may occur – routine blood screening and monitoring are not recommended but an urgent medical opinion should be sought if abdominal pain, nausea, dark urine or jaundice appear (see Table 3).

For atomoxetine, titration varies according to body weight. For children and young people who weigh less than 70kg, the recommendation is to commence at 0.5mg per kg daily for the first week and then increase according to response to 1.2mg per kg daily. Response to treatment should be assessed over the first 12 weeks.

Monitoring treatment

For both psychostimulants and atomoxetine, once an optimal dose has been reached, the child should be reviewed by the secondary care clinician at least every six months, including assessment of ongoing efficacy and adverse effects and measurement of growth, pulse and blood pressure using appropriate centile charts.[7] Regular communication with school is essential and use of parent and teacher rating scales, *eg* ADHD RS-IV[15] or SNAP-IV,[16] offer useful supplementary information.

Ideally, a local shared-care protocol between GPs and secondary care should be in place to delineate responsibilities for prescribing and monitoring.[7]

Lack of treatment response

If there has been no response to psychostimulants or atomoxetine, the diagnosis of ADHD and possible co-morbidity should be reviewed. Adherence to the medication schedule, side-effects and motivation should also be considered.[11] Discussion with a tertiary care centre regarding the use of higher doses of psychostimulants or referral for possible alternative medications, *eg* clonidine, guanfacine, bupropion, tricyclic antidepressants, could be considered. Psychological interventions can also be considered, particularly for children with co-morbid anxiety and ODD/conduct disorder.

Adverse effect	Management
Nausea, headaches, irritability, dizziness	May disappear spontaneously after first few days of treatment. Consider dose reduction or discontinuation if persists
Reduced appetite, weight loss and growth concerns	Administer medication with food. Advise extra snacks early in morning or later in evening. Provide dietetic advice on caloric augmentation. Consider dose reduction or omission at weekends or holidays. Consider referral to endocrinologist if growth significantly affected
Sleep difficulties (compare to baseline/ pretreatment pattern) (psychostimulants only)	Give "sleep hygiene" advice. Reduce evening dose or administer earlier in afternoon. Consider change to atomoxetine. Consider melatonin if pretreatment sleep difficulties
Tics (psychostimulants only)	Monitor pre- and post-treatment tics. Apparent worsening or onset may be temporary. If tics problematic or persistent (>3 months) change to atomoxetine
Tachycardia and hypertension	Small increases in pulse or BP are not unusual. If pulse and/or BP above 95th centile refer for investigation and consider dose reduction/discontinuation
Syncope suspected to have cardiac origin	Stop medication immediately and seek specialist advice
Dysphoria or agitation	Reduce dose and monitor effect
Suicidal thoughts (atomoxetine only)	Monitor carefully on initiation. Consider dose reduction or discontinuation if persistent
Somnolence (atomoxetine only)	Administer at different time of day or reduce dose
Jaundice, signs of liver disease or biliary obstruction (atomoxetine only)	Stop medication and seek urgent medical opinion

Table 3. Management of adverse effects of ADHD drug treatment

Follow-up

Along with physical monitoring, the effectiveness of and need for medication should be monitored regularly. Increases in dosage may be needed as the child grows. As the child moves through adolescence, the need for medication may reduce. Breaks from medication, *eg* over holiday periods, can offer a chance for growth to catch up but are also an opportunity for parents and adolescents

to review the need for medication. About 60–70 per cent of patients will have some ADHD symptoms into adult life[17] and there may be an ongoing need for medication, in which case a transition to adult mental health services should be planned as they approach late adolescence.

Conclusion

ADHD is a neurodevelopmental disorder with impairing and persistent symptomatology, which can impact adversely on learning, social relationships and emotional functioning in a significant proportion of the childhood population, with ongoing disadvantages in adulthood. Ongoing research is needed into many aspects of the disorder including effective treatment interventions. However, for the present, well-coordinated inter-agency working, behavioural management strategies and use of medication may help to mitigate the risks of ADHD.

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Declaration of interests

None to declare.

Dr Pickett is a consultant child and adolescent psychiatrist based in the West Centre, Glasgow