Use of stimulants for attention deficit hyperactivity disorder

Definitive diagnosis of attention deficit hyperactivity disorder is complex. David Coghill believes the condition is undertreated, but Harvey Markovitch argues that current uncertainties about diagnosis and treatment mean doctors should be cautious

FOR The consequences of persistent, pervasive, and disabling hyperactivity, impulsivity, and inattentiveness on a child's development and functioning are serious. The presence of attention deficit hyperactivity disorder (ADHD) or hyperkinetic disorder predicts a wide range of negative outcomes. These include poor self esteem, academic achievement, occupational status, peer relationships, and family functioning and increased injury rates, disruptive and antisocial behaviour, substance misuse, and mood and anxiety disorders.[1] As treatment can restore healthy functioning to many of these children and young people, a reluctance to diagnose ADHD seems unreasonable and withholding effective treatments from those who have had the condition diagnosed is unjustifiable.

Opponents of the validity of ADHD as a diagnosis cite our incomplete understanding of its precise biological basis. Sensationalist journalism has often caught public, and at times professional, attention by delivering negative messages about the "dangers" of stimulants such as methylphenidate and the sharp increases in use over the past decade. It is important, however, to examine this information in context.

The brain is the most complex of biochemical machines. The many technical and ethical constraints on studying its development and functioning make it unsurprising that we have no definitive causal models for any of the complex developmental psychiatric disorders. Indeed, it is impressive that we know as much as we do about the biological underpinnings of ADHD. Considerable convergent, replicated evidence now supports the role of complex polygenic and environmental factors in causing alterations in neural architecture and functioning; these changes result in a range of neuropsychological performance deficits and ultimately the behavioural symptoms associated with ADHD.[2]

Risks and benefits of stimulants

Scientific study shows that stimulants exert a positive effect on the biological and cognitive processes that are thought to cause ADHD. They improve the inhibition of inappropriate responses and cognitive flexibility and memory functioning[w1 w2] rather than "doping children up" or turning them into "zombies," as is often suggested in the media. Depression and emotional blunting are in fact uncommon but important adverse events with psychostimulants and respond to withdrawal of treatment.

ANNABELLA BLUESKY/SPL

Where's my stimulant?

Systematic reviews and meta-analyses of evidence from short term studies have all concluded that both methylphenidate and dexamfetamine are effective and safe.[3] Evidence from longer term studies, although still sparse, is starting to appear and supports continuing effectiveness and safety over the medium to long term.[w3] Importantly, neither methylphenidate nor dexamfetamine, both of which have been used for more than 50 years to treat the symptoms of ADHD in millions of children, have been associated with serious adverse events when used as a monotherapy, through either the pharmacovigilance systems or in peer reviewed journals.

More long term studies of psychostimulants are required. Before further progress can be made, however, the ethical and practical difficulties of designing and conducting such studies, and their high costs, must be acknowledged and tackled by researchers and funding bodies. One important recent finding warns of the broader risks and costs to the individual, the family, and society associated with undertreatment of ADHD. Huss and Lehmkuhl found a 50% reduction in rates of

P+ *References w1-w7 are on bmj.com*

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substance misuse in patients treated with stimulants compared with untreated patients.[4]

When and how should stimulants be used?

Recent studies have shown drug treatment has appreciable advantages over behavioural approaches and questioned the added effectiveness of a combined approach over drugs alone.[5] [w4] Evidence based and consensually driven clinical guidelines support the use of psychoeducational, pharmacological, and behavioural treatments for ADHD.[6–10] All propose that stimulants should be considered as potential first treatment, particularly for patients with the most severe, pervasive, and disabling symptoms. This does not exclude behavioural treatments, which remain an appropriate alternative first step in less severe cases (followed by a trial of drugs if ineffective) and as an adjunct to drugs in severe cases and in the management of associated and comorbid problems.

All the guidelines emphasise the need for a detailed, accurate, and comprehensive assessment by well trained and experienced specialist practitioners before starting treatment. In the United States, however, most treatment is carried out within a primary care setting with only a few patients ever having contact with a specialist services.[w5] As a consequence large variations in practice occur, and although only one in eight children with ADHD are treated with stimulants, half of those being treated do not meet the criteria for ADHD.[w6]

Attitudes and practice also vary widely across the United Kingdom. In Scotland, for example, prescription rates for stimulants vary sevenfold among health boards.[w7] Although variability in the quality of assessment results in some inappropriate prescription of stimulants, the main evidence is for under-recognition and undertreatment. The National Institute for Clinical Excellence, using a conservative approach to decision making on treatment, reported that in England and Wales only 30% of patients with hyperkinetic disorder, the most severe form of ADHD, were receiving stimulants.[7] Evidence suggests a similar situation in the rest of the United Kingdom. Thus, the increases seen in the prescription of psychostimulants over recent years represent less of a worrying explosion than a move towards better recognition and treatment of a serious childhood disorder.—David Coghill

Contributors and sources:DC runs an assessment and treatment service for children and young people with neuropsychiatric disorders and is involved in researching the neurobiolology and treatment of ADHD. This article arose from a BMJ/BNF sponsored debate on the use of medications to manage childhood behavioural disorders.

Competing interests: DC has been paid by Celltech, Janssen Cilag and Lilly for consultancy, research, and speaking at conferences and reimbursed by Janssen Cilag and Lilly for attendance at several conferences.

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AGAINST Doctors must take great care before prescribing psychoactive drugs for children. Relying on published trials and manufacturers' summaries of product characteristics (data sheets) has proved inadequate for selective serotonin reuptake inhibitors.[1] Doctors should be just as cautious before prescribing central nervous system stimulants for attention deficit hyperactivity disorder (ADHD) and consider their response to the fact that despite decades of use, the first reasonably large medium term controlled trial (14 months' use) was not published until 1999.[2]

Even though evidence of safety and efficacy is more qualitative than quantitative, overall prevalence of stimulant use may be as high as 6% in the United States. If we were to follow the American Academy of Pediatrics guidelines on treating school aged children with ADHD,[3] as many as 17% of all children would be treated.[4] Putting this alongside the National Institute for Clinical Excellence's recommendation that about 1% of UK children probably merit stimulants[5] raises questions.

Problems of diagnosis

Firstly, diagnostic criteria for the disorder differ widely. Some of the disparate figures mentioned above are explained by case series using either the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III-R or DSM-IV) or the International Classification of Diseases (ICD-10) for diagnosis.

Secondly, I contend that it is unlikely that most prescribers go through the extensive initial and follow up checklists recommended when starting and maintaining children on stimulants.[6] These include separate child and parental interviews, completion of a validated rating scale by parents and a teacher, and a teacher's report. Prescribers must check symptoms against one of the standard diagnostic lists and also check the child's social functioning and whether he or she has any comorbidity, such as depression. All of this is completed before the stimulant is given. In addition, parents should be taught handling skills and simple behavioural techniques. Parental and teacher ratings and reports of possible adverse effects should be repeated monthly for six months to inform dose titration.

There is no reason to disbelieve that specialist academic units, such as the one from which Hill and Taylor report,[6] proceed with such thoroughness and care. It would be asking too much to believe that all paediatricians, child psychiatrists, and general

practitioners follow suit, even if they had the time available to do so. Indeed, there is some evidence for this contention, at least in Australia and the United States. Rey and Sawyer looked at published surveys of community samples of children with ADHD or taking stimulants and concluded that 17.5-66% of participants taking stimulants did not have ADHD (and 12.1-86.7% of those with ADHD were being treated).[4]

Caution is needed

Evidence exists that stimulants are mostly safe and often effective. What is lacking is evidence that the right children are being treated. While there is so much disagreement about prevalence, confusion about how to distinguish ADHD from conduct disorders, and inconsistent guidelines, prescribers should tread warily. Paediatrics, like other specialties, is full of ideas that seemed good at the time. We have (I hope) stopped prescribing antihistamines to treat crying and sleeplessness in small infants, even though this was standard practice in the past. Cisapride was abandoned in haste, when its potential cardiac ill effects were defined, despite having been used extensively in treating children and even premature babies with gastro-oesophageal reflux. Most selective serotonin reuptake inhibitors are no longer recommended for children. If we do not take care, methylphenidate might meet a similar fate, even though it clearly benefits some children and their families.—Harvey Marcovitch

Contributors and sources: Harvey Marcovitch was a practising paediatrician for 25 years so was faced with many such children. Lack of resources meant that few had the luxury of a referral to child and adolescent mental health services. As press officer for the Royal College of Paediatrics and Child Health he has had to field constant, sometimes hostile, media inquiries and so has had to make himself familiar with the scientific literature on the subject.

Competing interests: HM is employed by BMJ Publishing Group but is unaware of any advantage to him of being invited to submit this paper. He once received a small fee for contributing to a debate on this subject.

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Managing comorbidities in patients at the end of life

James Stevenson, Amy P Abernethy, Cathy Miller, David C Currow

Chronic conditions require careful management in patients who develop a life limiting illness. Doctors need to consider both the physical and psychological effects of treatment

A 68 year old woman with extensive small cell lung cancer and rapid weight loss also has long term mild hypertension with no evidence of end organ damage. What would you do about her antihypertensive treatment?

a) Stop drug treatment because she has a terminal illness

b) Continue the drugs because you would not want her blood pressure to get worse (and the conversation about stopping them may be difficult because last year you told her she would be taking these drugs for the rest of her life)

c) Wait until she develops postural hypotension and then consider reducing her drugs

d) Reduce her drugs and watch carefully.

People with progressive life limiting illnesses are often also taking drugs for treatment or prevention of long term conditions.[1] However, little guidance exists to help clinicians consistently and systematically manage chronic comorbidity. Some clinicians stop drugs for chronic conditions arbitrarily because the person has a progressive life limiting illness. At the other end of the therapeutic spectrum, some clinicians do not stop any long term treatments until the patient is unable physically to take them or suffers adverse effects. Competent care for people with life limiting illnesses requires careful management of their long term drugs. We outline some key considerations.

Patients with life limiting illness

Life limiting illnesses include advanced cancer, end stage organ failure, neurodegenerative disease, and AIDS. Common conditions that need active management at the end of life include hypertension, atrial fibrillation, hypercholesterolaemia, thromboembolic disease, dementia, osteoporosis, diabetes mellitus, and arrhythmia. Patients may also be taking hormone replacement therapy, immunosuppressive therapy after transplantation, or drugs to prevent opportunistic infections in people who are immunocompromised. Both the life limiting illness and comorbidity change clinically over time and therefore need regular review. What is the best way to minimise the increasing risks of long term drugs as a person's body changes with advancing life limiting illness and the known risks of polypharmacy as additional drugs are introduced to control symptoms?[2]

Key considerations

Current and emerging evidence can help generate a framework to improve clinical decision making for the pharmacological and non-pharmacological management of common chronic conditions in patients at the

Illustrative clinical scenarios are presented on bmj.com

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