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Child and learning disability psychopharmacology

In January 1997, the British Association for Psychopharmacology convened a Round Table meeting to look at issues surrounding the prescription of psychotropic drugs to children or individuals with learning disabilities. This followed reports in the UK media about increasing rates of prescription to children with attention deficit hyperactivity disorder (ADHD) and children who are depressed as well as concerns regarding the prescription of psychotropic drugs to both children and adults with learning disabilities. The participants included both clinical and basic scientists, psychiatrists and psychologists, as well as regulators and representatives of the pharmaceutical industry and they were drawn from the UK, the United States, Canada, Holland, France and Germany. The brief was to consider the evidence in favour of prescribing for individuals with learning disabilities or children with obsessive–compulsive disorder, schizophrenia, depression or ADHD and the basis on which prescribing could take place in the absence of clinical trial evidence of efficacy drawn from the populations in question, where prescribing is effectively off label or outside the remit of a medicine's product licence or sometimes must take place in the face of data sheet disclaimers that it is contraindicated.

The current state of the evidence

Obsessive–compulsive disorder (OCD)

There are a number of clinical trials which indicate that clomipramine and other drugs which potently inhibit serotonin reuptake (the SSRIs) have a therapeutic utility in OCD presenting in children and that these agents are more effective in OCD than drugs selectively active on the noradrenergic system. Treatment, however, produces only a partial remission in some individuals and it must be maintained or relapse is likely (Flament, 1994). At present clomipramine and fluvoxamine have been granted and sertraline is seeking a product licence in the United States for use in children and adolescents with OCD. There was agreement that the indications of efficacy were sufficient to support pharmacotherapeutic approaches in childhood OCD even for children younger than the age stipulated in current licences, given the consistency with the findings in the adult field and the fact that OCD is a disorder that may have its onset in childhood. At present there are no contraindications and possibly advantages in combining pharmacotherapy and psychotherapeutic strategies.

Schizophrenia and other childhood psychoses

There is a consensus that schizophrenia is a condition that may begin in early adolescence and that it is as valid to prescribe neuroleptics (antipsychotics) for schizophrenic conditions beginning at this age as it is to prescribe them for adults with schizophrenia. Leaving the condition untreated is likely to enhance later deterioration, whereas effective treatment may enable normal development to continue or to be re-established. There are concerns in the area of treatment of the childhood psychoses with neuroleptic drugs, as these agents and in particular the 'typical' antipsychotics, are associated with significant risks of extrapyramidal symptoms (EPS) and tardive dyskinesia (TD). Current prescribing practices for these compounds are largely uninformed by research data on optimal therapeutic regimes and as a consequence the possibility of side-effects is probably increased. There is also some impression that prescribing may be constrained by cost considerations, so that older drugs, more likely to produce these side-effects, are used in preference to newer drugs which are less likely to produce problems.

There are, in addition, a range of psychotic conditions that occur pre-pubertally some of which may be linked to pervasive developmental disorders. At present there is little consensus as to the best method of handling these disorders in part because there is a lack of clarity as to the continuity between these conditions and adult schizophrenic or non-schizophrenic psychotic conditions and in part because there is a paucity of clinical trials in this area, although both neuroleptics and SSRIs have been shown in double-blind trials to have a clinical utility in autistic disorders. Given the present state of the evidence, prescribers should weigh carefully the benefits of treatment against the risks posed by neuroleptic compounds and possibly explicitly justify the regimens they propose.

Depression

At present there are some indications that there may be a discontinuity between pre-pubertal 'depression' and both post-pubertal and adult depression. In addition, there appear to be some differences between the forms of depression that occur post-pubertally to those that occur in adulthood. Some bipolar affective disorders and unipolar depressive disorders clearly may have their onset in adolescence and as such the same basis for prescribing exists in these conditions as in OCD and schizophrenia, i.e. the conditions do not simply have an onset after the age of 18 years even though at present the evidence of

efficacy is largely drawn from subjects between the ages of 18 and 65 years.

However, treatment studies conducted in adolescents with depressive disorders have indicated a very high rate of placebo response in studies designed to test the effectiveness of both antidepressant and psychotherapeutic strategies. The reason for such high rates of response to non-specific interventions is at present not clearly understood. One possibility is that there is considerable heterogeneity among teenage depressions with some being continuous with adult forms of depression while others are more situationally determined and have more in common with emotional reactions. Even in more 'melancholic' pictures, however, placebo response rates can be considerable. At present, there is no evidence for effectiveness of tricyclic antidepressants in these populations. There is emerging evidence from case reports and clinical trials that SSRIs may be effective (Birmayer *et al.*, 1996; Emslie *et al.*, 1997). The optimal clinical management of depressive conditions in childhood and adolescence, therefore, will require opportunities for extended assessment of the presenting condition, monitoring of treatment response as well as possibilities for multi-modal treatment strategies.

Attention deficit hyperactivity disorder (ADHD)

This condition was first described in 1902 by Stil. In 1937 following the synthesis of dexamphetamine 2 years previously, the first reports emerged that a stimulant might be useful in the management of the condition. Among the first double-blind placebo control trials done in psychiatry, one looked at the usefulness of methylphenidate for the condition and found it to be effective. Since then an extensive literature has emerged to support the usefulness of stimulants (methylphenidate, dexamphetamine and pemoline) in the management of ADHD. There are close to 100 independent studies almost uniformly pointing to the effectiveness of the medication in this condition in the short-term, and to a benefit to the child in terms of their functioning at home, in school and socially. There is a low rate of treatment-emergent problems and addiction to stimulants as a result of treatment does not at present appear to be a problem in this condition; indeed there are some indications that treatment may reduce the likelihood of later substance dependence (Klein, 1987).

At present the weight of evidence makes this one of the better supported treatments in medicine. However, at a time when practice is supposed to follow scientific evidence, there is considerable variation in what happens in practice both between countries and within a country such as the UK. It can be noted that there appear to have been campaigns in the United States and the UK denigrating the effectiveness of the treatment and the validity of its use. Historically there would appear to have been some reluctance to prescribe psychotropic medicines to children; the nature of this reluctance remains unclear. There have been concerns that diagnosis may stigmatize. In addition, until recently prescribing has had to take place in the face of disclaimers on medicine data sheets. It may also have been constrained by the fact that until recently few mental health professionals in the field of child psychiatry have had a training in psychopharmacology.

To date there are no non-pharmacological treatments which can substitute for stimulants in stimulant-responsive cases but a response to stimulants should be seen as enhancing the likelihood that other interventions will be successful where these are called for rather than as a substitute for all other therapies.

Learning disabilities

The difficulties experienced in prescribing off-licence, without the expressed consent of the taker of the medication and unsupported by clinical trial evidence drawn specifically from the population to whom the agent is being given also face clinicians in the area of learning disabilities. The problems are compounded in this field in that very often the clinical syndromes will differ from those found in both child and adult psychiatry and, owing to communication difficulties with their patients, diagnosticians will need to focus almost exclusively on observable behaviours. It will be relatively unusual, therefore, for subjects to meet formal diagnostic criteria for OCD, affective disorder, schizophrenia or other psychoses or ADHD. Nevertheless following assessment, prescribing will often proceed if there are some indications that these syndromes are present. Prescribing is justifiable based on a similar extrapolation to that which applies in child psychiatry. In these circumstances and particularly in cases where elements of general adult syndromes are not readily discriminable it would be prudent to monitor closely the effects of prescription and to continue with treatment only if benefits can be demonstrated.

Concerns in the learning disabilities field have also arisen owing to what has appeared at times to be the use of antipsychotic medication for the purposes of behavioural control, whether to minimize aggression or reduce self-harm. This has led to legal and media attention particularly in the United States and to the establishment of guidelines for assessment and treatment (Kalachnik, 1996). At present there are no clear indications that prescribing is inappropriate and there are a number of adequately-controlled trials supporting the use of neuroleptics, lithium and drugs active on the serotonergic system for disturbances involving aggression in patients with learning disabilities. In community and institutional facilities, however, cultures favouring early prescription may develop in response to behavioural events in patients with learning disabilities, the origin of which at present remains uncertain as does the impact of prescribing. One study has demonstrated that it is possible to reduce prescription rates or treatment levels in a proportion of cases in such settings without undue adverse consequences.

Diagnosis

There have been concerns that diagnosing a psychiatric condition in children and managing that condition with psychotropic agents will in some way disadvantage patients. A review of the evidence did not suggest this to be the case, although it must be remembered that any diagnosis in any area of medicine may be wrong. A good diagnosis and effective management was thought to be more likely to be enabling than

leaving conditions of moderate severity untreated. A diagnosis, even for example in the case of AIDS, may allow affected individuals and their relatives to lobby for resources and to ensure that the best available treatments are accessed in a manner that will break down stigma. It is the behaviour of the affected child that is likely to lead to stigma rather than diagnosis and treatment, particularly if treatment leads to an improvement in behaviour.

Shared care

In the UK as in many countries there is continued development in the roles of family health care teams. This offers opportunities for the management of patients in the community through shared care. Delivering shared care of high quality depends on the presence of adequate specialist care services to support primary care, on standards for care delivery and on the education of primary care medical and non-medical professionals on aspects of psychopharmacotherapy. Individual general practitioners will not see sufficient numbers of children with the range of learning disabilities or childhood psychiatric conditions to develop expertise in their management. Therefore initial management should commence within specialist services and subsequent management will require specialist services to support primary services through monitoring. Rational resource allocation would be supported by good evidence of clinical effectiveness and the development of such evidence in British clinical practice would be welcomed.

Prescribing

There is an impression that, except in the case of ADHD, there is considerably more evidence of efficacy for psychotropic agents in the field of adult psychiatry than in either the fields of child psychiatry or learning disabilities and on this basis prescribing in adult populations is more rational. This impression stems from the fact that pharmaceutical companies do their controlled trials in adult populations, owing to the greater prevalence of the conditions being investigated in these populations and in part owing to difficulties in obtaining consent in non-adult populations. This state of affairs is likely to persist.

However, the adult populations that are studied are selected to be relatively free of complications. Therefore, for instance, the act of prescribing antidepressants in cases of depression where the individual may be severely depressed, suicidal, otherwise physically ill or on a combination of other treatments, always requires an extrapolation from the database that has been generated in the clinical trials put together in pursuit of a licence. The situation as regards prescribing in child psychiatry or learning disabilities, where the condition is continuous with the general adult condition, is in principle the same—it requires an extrapolation from a database put together to demonstrate that a claim that efficacy in depression is not unwarranted.

There is a great lack of clarity about the meaning of a licence that a company is offered. Many clinicians in the UK and France appear to think that they cannot prescribe off-licence—that it would be almost illegal to do so and that they would be exposing themselves to considerable risks of litigation. In fact, the Medicines Act and the EC Pharmaceutical Directive 89/341/EEC allows doctors to prescribe unlicensed medicines or to use licensed medicines for indications or in doses or by routes of administration outside the recommendations of the licence as well as to override warnings or precautions given in a licence (British Paediatric Association, 1996).

Licences primarily constrain the claims a pharmaceutical company can make rather than clinical practice. Even product labelling stating that prescribing is contraindicated in the paediatric age range is primarily meant to constrain company claims rather than to limit the freedom of prescribers. There are regulatory and other moves to encourage the pharmaceutical industry to provide evidence for the effectiveness of their compounds in paediatric conditions and moves to recast the labelling so that it will represent whatever evidence is available in childhood populations rather than baldly state that prescribing is contraindicated.

While getting to market requires a demonstration of efficacy rather than efficacy in all circumstances, the sponsors of trials will almost inevitably opt for the least complicated situation in which to demonstrate efficacy. In the face of this situation there must also be some onus on funding bodies and clinicians to provide independent evidence. Funding for and interest to undertake independent clinical trials is particularly poor in the UK at present, even in general adult psychiatry.

Good practice

In both the fields of learning disabilities and child psychiatry there would appear to have been some tendency, whether for ideological reasons or for convenience or owing to a lack of training, to adopt one therapeutic approach, be it pharmacotherapeutic or psychotherapeutic, and to adhere to it exclusively even in the face of non-response. This has left the relatives of patients in the difficult position of having to seek second opinions or treatments, sometimes outside orthodox channels; it has required them on occasion to challenge overzealous treatment where the risks of treatment appear to outweigh the benefits that might accrue from it. Such situations might be avoided if therapists, of whatever persuasion, specified at the outset of treatment what a reasonable period might be for a treatment trial for each patient, how they would monitor the outcome of treatment, what the expected adverse events are and what they would do in the event of non-response at the end of the trial period. It would also help if patients and their carers had access to better information on treatment alternatives.

There is a sense that in both the fields of child psychiatry and learning disabilities there is a renewed interest in generating evidence as regards the effectiveness or otherwise of treatment approaches. It is hoped that resources will follow

demonstrations of efficacy as the problems of assessment and monitoring of on-going treatments in both these areas will require a greater input in terms of resources than the management of comparable disorders in the adult field require. Demonstrations of efficacy should be taken as providing opportunities for multi-disciplinary collaboration to ensure optimal outcomes rather than a closure on the need for funding.

Training

There is a strong perception within the UK that training in psychopharmacology for medical personnel operating in the fields of child psychiatry, paediatrics and learning disabilities has lagged behind the training offered in the United States or that in the adult field within the UK. Bodies responsible for the provision of training and for fostering a climate in which such training was conducted appropriately and valued should be aware of this situation.

Summary

The treatment of children and individuals with learning disabilities, both adults and children, with drugs has been hampered by a lack of adequately conducted trials. More studies are called for. Until such time, the justification for treatment will rest primarily on an extrapolation from known treatment responses in adult populations. This appears clearly justified in the case of schizophrenia and OCD. Treatment of the affective disorders is less clearcut and provides grounds for caution. In some conditions that do not have exact adult parallels, such as ADHD, specific treatments can be recommended. In others associated with pervasive developmental disorders treatment may need to proceed on a case by case basis. In all cases treatment choices should be demonstrably safe and progress on treatment monitored.

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Appendix 1: List of participants

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