Medication prescription for depression in children and adolescents

Treating depression in young people is a challenge. The treatment of choice until very recently has been medication with selective serotonin reuptake inhibitors (SSRIs). It was therefore dismaying when the Medicines and Healthcare Products Regulatory Agency in the UK issued a warning that SSRIs are largely ineffective in the treatment of major depression in children and adolescents, and may cause suicidal behaviour and self-harm.¹

Regulatory agencies issued a general advisory regarding the increased risk of suicide in paediatric use of all SSRIs.²

There are several disturbing elements in this scenario: Firstly, to obtain registration of a drug, companies in Canada are compelled to submit all research data to the regulatory authority, but are not compelled to publish it. Many results are therefore not in the public domain. Secondly, research on SSRI therapy for young people with depression is characterised by high placebo response rates. In one trial, 69% of patients improved on medication, compared with 59% on placebo. This may not be known to prescribers or patients.

Other points worthy of note include:

- The gap between the quality of evidence needed to get a drug registered and the actual treatment of patients: a first episode of major depression may last for as long as 7 - 9 months and may recur, while the typical period of a controlled trial is 6 - 8 weeks.
- Postmarketing surveillance of safety and effectiveness leaves much to be desired. Reports obtained directly from patients and relatives have uncovered previously unrecognised adverse drug effects. Most reporting systems lacked important information such as the patient’s history and the drug dosage.
- Many of the trials left out remission, the most important outcome measure, and did not include patients’ self-rating of depression, parents’ ratings, global psychiatric symptoms or global functioning.
- Patients and their families should be informed that antidepressants will not cure the depression, and at most might improve some depressive symptoms.

Garland³ suggests that physicians treating children with recent onset of depression should commence with education regarding sleep hygiene, exercise, practical coping skills and family interventions. They should provide the frequent supportive contact typical of clinical trials. Psychosocial therapy, cognitive therapy and interpersonal therapy are also suggested.

After a period of careful observation and a trial of non-pharmacological therapies, children with persistent depression or co-morbid anxiety disorders may require treatment with medications. Physicians should choose a SSRI that has been approved for use in children and adolescents, such as fluoxetine for depression or sertraline for obsessive-compulsive disorder.

Physicians should also be alert to the fact that the psychiatric adverse effects of SSRIs overlap with manifestations of depression itself, which may tempt a physician into (incorrectly) increasing the dosage of the medication.

Patients and their families should be informed that psychiatric or behavioural adverse effects are almost as likely as antidepressant effects.

Two suggestions arise from the two articles:

1. Regulatory requirements for evidence of efficacy should adequately reflect the key outcomes of importance to patients. Informed consent for participation in trials should be based on full knowledge and unrestricted access to all the results of clinical trials.¹

2. Practice guidelines need to be rewritten to reflect a critical analysis of the full body of evidence, both published and unpublished.

Leading psychiatrists in the UK are, however, expressing misgivings about the regulatory action to curb the use of SSRIs in young people with depression. The Royal College of Psychiatrists Faculty of Child and Adolescent Psychiatry has written to equivalent organisations in the USA and Europe to stress its concern about the warning that was issued by the UK Committee on Safety of Medicines (CSM). They are querying the validity of the data.¹

To allow clinicians to assess the evidence for themselves, CSM has released the drug company data it used to review safety and efficacy of SSRIs, which may clarify the picture somewhat, although many physicians have no idea of how to analyse these data. The CMAJ asked John Geddes, Professor of Epidemiological Psychiatry at Oxford University, to check the data, and his verdict was, ‘I don’t think the analysis is up to the current best standards ... If this was sent to a journal, it would not do well in peer review.’

The last word goes to David Healy, a psychiatrist in North Wales, who has written on SSRI safety for many years, and gave evidence to the CSM investigators: ‘The trials assessed by the CSM clearly show that children taking SSRIs for depression are more likely to become suicidal than those taking a placebo.’³

Currently, no SSRIs are licensed for the treatment of depression in under-18s in the UK.

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