

Depressed youth, suicidality and antidepressants

No cause for panic, but an incentive to improve clinical practice

The use of selective serotonin reuptake inhibitors (SSRIs) in depressed children and adolescents has received considerable attention in the past year; this attention has included concerns about increased suicide risk, revised evidence about effectiveness, growing prescription numbers, and revelations of drug companies withholding data.¹ The discovery of unforeseen risks in other drugs such as cyclooxygenase-2 inhibitors has intensified the climate of uncertainty and mistrust about drug treatment. Some argue that to diagnose major depression in children is to medicalise the unhappiness caused by affluence, permissiveness, a decaying family and society.² By contrast, medical practitioners and governments have been told during the last quarter century that depression is a serious illness that can lead to suicide, poor physical health, and personal, professional and social difficulties. Thus, the Australian community has invested considerable resources in trying to tackle this scourge (eg, The National Depression Initiative³). If experts disagree, it is little wonder that the public and clinicians are confused, yet severely depressed teenagers continue to come to doctors for management.

Do SSRIs increase the risk of suicide?

Although SSRIs have been used “off label” in children and adolescents from the early 1990s, none is formally approved for paediatric depression in Australia. Evidence of benefit is ambiguous enough for scholars to be divided,^{1,4} and we do not discuss it here.

Findings of the few epidemiological and ecological studies available conflict about suicide risk. First, SSRIs are less toxic than the older tricyclic antidepressants, particularly in overdose.⁵ Second, youth suicide rates, after rising for about 40 years, inexplicably declined in Australia and other Western countries in the late 1990s.⁶ While its cause is probably multifactorial in origin, the decline correlates with increasing SSRI use.⁷ More prescriptions did not result in higher suicide rates, as might have been expected if SSRIs induce suicide, although this might have been disguised within the general decline.⁸ Third, SSRIs are not found more often than expected in post mortem examinations of people who have committed suicide.^{9,10} Conversely, some studies suggest that deliberate self-harm (DSH) episodes are slightly increased in adults taking SSRIs.^{11,12} Another study reported elevated suicidal behaviour during the first month of tricyclic antidepressant or SSRI treatment¹³ (this was not replicated in the paediatric trial data¹⁴). Clinicians have long recognised an increased risk of suicide in patients starting antidepressant treatment.

A recent review commissioned by the Food and Drug Administration (FDA) of 24 controlled trials with more than 4400 children and adolescents showed a higher incidence of suicidality (suicidal thoughts, attempts) in those receiving antidepressants (4%), mostly SSRIs, compared with placebo (2%).¹⁴ There were no known suicides. Despite methodological shortcomings (eg, post hoc analyses, varying trial methods, suboptimal assessment of suicidality, exclusion of suicidal youth), this effect seems robust, if

small (2%). Thus, the FDA issued the latest in a series of advisories about suicidal behaviour in children and adolescents treated with antidepressants, recommending the strongest labelling warnings, but not contraindicating their use.

The meaning and mechanisms underlying increased suicidality in those taking antidepressants are unclear. Suicidal behaviour results from complex interactions in which individual and psychosocial factors, as well as depression and other mental health problems, play a role. In the review commissioned by the FDA, SSRIs induced akathisia, agitation, and irritability more often than placebo.^{14,15} Patients with these symptoms, often described as “activation”, were up to seven times more likely to show suicidality than those without activation.¹⁴ Like other antidepressants, SSRIs can trigger manic switches, often with unstable mood and higher suicide risk. Sex, age, history of suicide attempt, and non-completion of the trial did not influence suicidality, but statistical power was weak because of low numbers.¹⁴ It is also possible that non-compliance, which may set off withdrawal symptoms,¹⁵ plays a part.

Handle with care

Growing knowledge about the risks of antidepressants is an incentive to improve clinical practice for a disorder that, if left untreated, is associated with significant morbidity and mortality. Large increases in the use of SSRIs in adolescents and children suggest we have become casual about prescribing them. We may be giving SSRIs to mildly depressed adolescents and neglecting regular review, counselling, and cognitive behaviour therapy (CBT). The association between “activation” and suicidality highlighted above¹⁴ emphasises the importance of monitoring and managing side effects, which are dose-related.¹⁵

As in all medicine, practice should be guided by a careful appraisal of benefit and risk based on best external evidence and individual clinical experience. While the credibility of antidepressant medications has been undermined, evidence for CBT and related treatments has not received the same level of scrutiny, and is flimsy for moderate and severe depression,¹⁶ particularly in non-research settings. Besides, psychosocial treatments require more cooperation from depressed teenagers who are often hostile, unmotivated, demoralised, or lack insight. This could easily lead to therapeutic nihilism or a regression to treating depression primarily as a moral or social problem.²

There is no definite answer yet about whether to prescribe or not; clinicians must weigh the pros and cons for each patient. Children and families must be informed of the risks of medication — parents who believe their children killed themselves because they were taking SSRIs consistently complain they “were not told”. Until the ambiguities are resolved, based on our clinical experience, we believe that SSRIs (chiefly fluoxetine¹) can be considered, but only for severe depression, when it produces serious impairment and fails to respond to psychosocial treatment over a few weeks. Combining SSRIs and CBT may be more effective, and might reduce suicide risk¹⁷ However, apprehension about SSRIs

should not lead us back to using tricyclic antidepressants (which are more toxic), to blaming sufferers or their families, or to refusing to treat depressed adolescents at all.

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