

Depressed youth, suicidality and antidepressants

Robert D Goldney

Professor of Psychiatry, University of Adelaide, The Adelaide Clinic, 33 Park Terrace, Gilberton, SA 5081. Robert.goldney@adelaide.edu.au

TO THE EDITOR: Two recent items in the Journal might potentially lead to misinterpretation of the evidence on managing depression in young people.

The first was the book review entitled *Darker side of "wonder drugs"* by Jureidini¹ in which there was no disclosure that the author of the review is president of Healthy Skepticism, a body which has been quite strident in its opposition to antidepressant therapy. The second was the unattributed comment in the editorial by Rey and Dudley describing "parents who believe their children killed themselves because they were taking SSRIs [selective serotonin reuptake inhibitors]..."² which may imply subtly that this has occurred frequently.

In a review of the United Kingdom General Practice Research Database of more than three million people,³ there were no suicides among the 6976 aged 10–19 years who had been prescribed one of two SSRIs or two tricyclic antidepressants; however, 15 people in that age group who had not received an antidepressant drug died by suicide. Furthermore, in a review of 14857 suicides in Sweden, of the 52 involving people under 15 years, no SSRIs were detected, and in the 15–19-years age group, those taking SSRIs had a lower relative risk of committing suicide than those taking other antidepressants.⁴

Clinicians with responsibility for children and adolescents can be reassured by these data, and also by the fact that the American Food and Drug Administration "black box" warning (their most potent warning) about antidepressants has recently been modified.⁵ Furthermore, the American Academy of Child and Adolescent Psychiatry and the American Psychiatric Association have provided a new resource about the use of medication in treating childhood and adolescent depression,⁶ which has been endorsed by over a dozen United States organisations comprising a "national coalition of concerned parents, providers, and professional associations". This should allay questions that have rightly been raised, but that have been answered in favour of the judicious use of antidepressants, along with other therapeutic measures for children and adolescents with severe depression.

In view of the strong association between child and adolescent mood disorders and suicide,⁷ the above research findings and the recommendations of respected professional bodies raise the issue of potential legal action for not at least trialling antidepressant medication in young people with severe depression if non-pharmacological measures are ineffective.

Competing interests: I have received honoraria and research grants from a number of pharmaceutical companies for presentations and research on depression.

- 1 Jureidini JN. *Darker side of "wonder drugs"* [book review]. *Med J Aust* 2005; 182: 293.
- 2 Rey JM, Dudley JM. Depressed youth, suicidality and antidepressants. *Med J Aust* 2005; 182: 378–379.
- 3 Jick H, Kaye JA, Jick SS. Antidepressants and the risk of suicidal behaviors. *JAMA* 2004; 292: 338–343.
- 4 Isacson G, Holmgren P, Ahlner J. Selective serotonin reuptake inhibitor antidepressants and the risk of suicide: a controlled forensic database study of 14857 suicides. *Acta Psychiatr Scand* 2005; 111: 286–290.
- 5 Hanson E. AACAP/APA Press conference introduces new guides for educating parents, consumers about antidepressants. *Am Acad Child Adolesc Psychiatry News* 2005; 36: 60–61.
- 6 American Psychiatric Association and American Academy of Child and Adolescent Psychiatry. The use of medication in treating childhood and adolescent depression: information for patients and families. Available at: <http://www.parentsmedguide.org> (accessed May 2005).
- 7 Shaffer D, Gould MS, Fisher P, et al. Psychiatric diagnosis in child and adolescent suicide. *Arch Gen Psychiatry* 1996; 53: 339–348. □

Peter R Mansfield,* Melissa K Raven,†
Jon N Jureidini‡

* Research Fellow, University of Adelaide, SA;
† Lecturer, Flinders University, Adelaide, SA; ‡ Head,
Department of Psychological Medicine Women's and
Children's Hospital, Adelaide, SA.
peter.mansfield@adelaide.edu.au

TO THE EDITOR: Rey and Dudley cite clinical experience as the basis of their recommendation of selective serotonin reuptake inhibitors (SSRIs) — chiefly fluoxetine — for youth with severe depression plus severe impairment or failure of non-drug therapy.¹ They do not discuss the evidence on efficacy because they claim that it is "ambiguous enough for scholars to be divided". It is true that industry-funded scholars are continuing to suggest that SSRIs (chiefly fluoxetine) provide a worthwhile benefit.² However, the evidence is unambiguous. The four published comparisons of fluoxetine versus placebo for children and adolescents have all been negative on their pre-specified primary endpoints.^{3,4} A tiny average benefit is likely, but the magnitude of this benefit is unlikely to exceed the

magnitude of less frequent but more severe harms. Furthermore, the common clinical impression of worthwhile benefit is to be expected given the large average improvements seen in placebo groups.

Rey and Dudley speculate that psychosocial treatments may be less effective with uncooperative teenagers.¹ However, that group may also be at higher risk of the dangers of intermittent use of, and overdosing with, antidepressant drugs.

Rey and Dudley cite Timimi's critique of the concept of childhood depression⁵ as supporting "treating depression primarily as a moral or social problem". However, Timimi did not even allude to depression as a moral problem, and advocated a multi-perspective approach that normalises emotional responses to adverse life experiences and includes interventions addressing biological factors, such as diet, exercise, and cognitive abilities. Rey and Dudley use a related straw-man argument in their final sentence when they suggest that the only alternatives to SSRIs are tricyclic antidepressants, victim blaming, and non-treatment.

Rey and Dudley deny being influenced by the gifts and funding that they have received from drug companies. There is compelling evidence that gifts and funding are effective, on average, for influencing beliefs, especially among people who have an illusion of invulnerability.⁶ We are not aware of any way that any individual can know that he or she has not been influenced.

Competing interests: We are all office bearers in Healthy Skepticism, an international non-profit organisation whose main aim is to improve health by reducing harm from misleading drug promotion.

- 1 Rey JM, Dudley MJ. Depressed youth, suicidality and antidepressants. *Med J Aust* 2005; 182: 378–379.
- 2 March JS, for the TADS Group. Authors of TADS study reply to letter raising concerns. *BMJ* 2005; 330: 730–731.
- 3 Jureidini JN, Doeckel CJ, Mansfield PR, et al. Efficacy and safety of antidepressants for children and adolescents. *BMJ* 2004; 328: 879–883.
- 4 Jureidini J, Tonkin A, Mansfield PR. TADS study raises concerns. *BMJ* 2004; 329: 1343–1344.
- 5 Timimi S. Rethinking childhood depression. *BMJ* 2004; 329: 1394–1396.
- 6 Katz D, Mansfield P, Goodman R, et al. Psychological aspects of gifts from drug companies. *JAMA* 2003; 290: 2404–2405. □

Joseph M Rey,* Michael J Dudley†

* Professor, Psychological Medicine, University of Sydney, PO Box 142, North Ryde, NSW 1670. † Senior Lecturer in Psychiatry, University of New South Wales, Randwick, NSW.
jrey@mail.usyd.edu.au

IN REPLY: The data available are inconclusive, but suggest that treatment with selective serotonin reuptake inhibitors (SSRIs) may increase the short-term (less than 14 weeks) risk of suicidal thoughts or self-harm in children and adolescents slightly, by about 2%. However, SSRI treatment may actually decrease the number of completed suicides,¹ as Goldney also highlights. To show whether SSRIs influence the risk of completed suicide, a rare event, requires a randomised trial including up to two million individuals.² This will not happen. Hence, clinicians must rely on accumulated data from experimental, epidemiological, and observational studies. Disagreements about interpretation will doubtless continue.

In response to Mansfield and colleagues, we personally know of media reports influencing some practitioners to revert to using tricyclic antidepressants, and child psychiatrists to avoid treating depressed adolescents. We do not shrink from our interpretation of the implications of Timimi's reconceptualisation of "depression" as "unhappiness". Regardless of how childhood depression is classified or named, we remain concerned that the impetus for clinicians to diagnose and treat it not be lost. Its social correlates include stigma and racism, which often involve seeing mental health problems as moral failures of character.

Our view is that fluoxetine shows a favourable harm–benefit profile in moderate to severe depression. According to the Treatment for Adolescents with Depression study,³ which was not funded by drug companies, four children need to be treated with fluoxetine for one to show much or very much improvement attributable to medication. This compares with having to treat 21 children for one to display a widely defined harm-related event. The numbers improve further when fluoxetine is combined with cognitive behavioural therapy (3 and 50, respectively). Pending new studies, clinicians would be unwise to ignore these data when treating serious depression in young people, a recurring illness that produces much suffering, physical and psychosocial disability, and suicide (odds ratio estimates ranging from 11.0 to 27.0).⁴ Our opinions are consistent with those of the recently released joint clinical guidance by the col-

leges of psychiatrists, general practitioners, and physicians.⁵

Mansfield and colleagues suggest that our editorial's content might have been influenced by drug company gifts. We provided the educated readers of the Journal with information to judge this for themselves.

Competing interests: Joseph Rey was a member of the advisory committee for Strattera (Eli Lilly) and Concerta (Janssen-Cilag) and was funded by Eli Lilly to attend an international conference. Michael Dudley attends Pfizer-sponsored peer review dinners, and has (before the recent debates about drug company gifts) received bags, pens, and a CD.

- 1 Isacson G, Holmgren P, Ahlner J. Selective serotonin reuptake inhibitor antidepressants and the risk of suicide: a controlled forensic database study of 14 857 suicides. *Acta Psychiatr Scand* 2005; 111: 286-290.
- 2 Gunnell D, Saperia J, Ashby D. Selective serotonin reuptake inhibitors (SSRIs) and suicide in adults: meta-analysis of drug company data from placebo controlled, randomised controlled trials submitted to the MHRA's safety review. *BMJ* 2005; 330: 385-388.
- 3 Treatment for Adolescents with Depression Study (TADS) Team. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression. *JAMA* 2004; 292: 807-820.
- 4 Beautrais A. Risk factors for suicide and attempted suicide among young people. *Aust N Z J Psychiatry* 2000; 34: 420-436.
- 5 Royal Australian and New Zealand College of Psychiatrists, Royal Australian College of General Practitioners and Royal Australasian College of Physicians. Clinical guidance on the use of antidepressant medications in children and adolescents. Available at: <http://www.ranzcp.org/publicarea/pracguid.asp> (accessed Jun 2005). □

Duncan Topliss

Chairman, Adverse Drug Reactions Advisory Committee, Therapeutic Goods Administration, Department of Health and Ageing, Canberra, ACT 2601.
adrac@health.gov.au

COMMENT: Three essentially independent reviews of the use of selective serotonin reuptake inhibitor (SSRI) antidepressants in children and adolescents have been undertaken in Australia in the past 9 months.¹⁻³ The review by the Adverse Drug Reactions Advisory Committee¹ had input from representatives of the Royal Australian and New Zealand College of Psychiatrists and the Division of Paediatric and Child Health, Royal Australasian College of Physicians (RACP).

All three reviews noted the paucity of information to support the efficacy of these and other antidepressants in children and adolescents, and the frequent observation of increased suicidal thoughts and self-harm in clinical trials.

The colleges' review² and the National Prescribing Service Rational Assessment of

Drugs And Research (RADAR) review³ support the ADRAC advice that:

Any use of SSRIs in children and adolescents with MDD [major depressive disorder] and other psychiatric conditions should be undertaken only within the context of comprehensive management of the patient. Management should include careful monitoring for the emergence of suicidal ideation and behaviour which may particularly develop early in therapy, or if therapy is interrupted or irregular because of poor compliance. Cognitive behaviour therapy, if it is available, may enhance the outcome in MDD.

An SSRI should be chosen for a child or adolescent with MDD or other psychiatric condition only after taking into account the recent evaluations of clinical trial data and the Australian product information. Prescribers should be aware that the marketers of fluvoxamine and sertraline (indicated for obsessive compulsive disorder) advise against their use in children and adolescents with MDD, and the marketers of citalopram, escitalopram, paroxetine, venlafaxine and fluoxetine warn or caution against their use in patients aged less than 18 years for any indication.

It is important to note that children and adolescents who are being treated for MDD with an SSRI should not have their medication ceased abruptly.

- 1 Adverse Drug Reactions Advisory Committee. Use of SSRI antidepressants in children and adolescents. *Aust Adverse Drug Reactions Bull* 2004; 23: 22. Available at: <http://www.tga.gov.au/adr.aadrb/aadr0412.pdf> (accessed Jul 2005).
- 2 Royal Australian and New Zealand College of Psychiatrists, Royal Australian College of General Practitioners and Royal Australasian College of Physicians. Clinical guidance on the use of antidepressant medications in children and adolescents. Available at: <http://www.ranzcp.org/publicarea/pracguid.asp> (accessed Jul 2005).
- 3 National Prescribing Service RADAR. Selective serotonin re-uptake inhibitors in child and adolescent depression. April 2005. Available at: <http://www.npsradar.org.au/npsradar/content/SSRIs.pdf> (accessed Jul 2005). □