

Saturday 19 February 2005



Suicide, depression, and antidepressants

Patients and clinicians need to balance benefits and harms

Papers pp 385, 389,
396

Unipolar depression, one of the most important causes of disability worldwide,¹ is characterised by depressed mood, hopelessness, helplessness, intense feelings of guilt, sadness, low self esteem, thoughts of self harm, and suicide. Up to 15% of patients with unipolar depression eventually commit suicide.² Although clinical guidelines recommend treating moderate to severe depression with antidepressant drugs,³ debate persists on whether some antidepressant drugs, in particular the selective serotonin reuptake inhibitors (SSRIs), cause the emergence or worsening of suicidal ideas in vulnerable patients. New insights on this key issue have been provided by three articles published in this issue.

Fergusson et al conducted a systematic review of published randomised controlled trials comparing SSRIs with either placebo or other active treatments in patients with depression and other clinical conditions.⁴ They found an almost twofold increase in the odds of fatal and non-fatal suicidal attempts in users of SSRIs compared with users of placebo or other therapeutic interventions (excluding tricyclics). No increase in risk was seen, however, when only fatal suicidal attempts were compared between SSRIs and placebo. Finally, no differences were observed when overall suicide attempts were compared between users of SSRIs and tricyclic antidepressants.

By contrast, Gunnell et al included in their review both published and unpublished randomised controlled trials submitted by pharmaceutical companies to the safety review of the Medicine and Healthcare products Regulatory Agency.⁵ These trials compared SSRIs with placebo in adults with depression and other clinical conditions. Three outcome measures were studied: completed suicide, non-fatal self harm, and suicidal thoughts. The researchers found no evidence for an increased risk of completed suicide, only weak evidence of an increased risk of self harm, and inconclusive evidence of an increased risk of suicidal thoughts (estimates compatible with a modest protective or adverse effect).

Finally, the nested case-control study reported by Martinez et al, based on information extracted from the General Practice Research Database, analysed the risk of non-fatal self harm and suicide in patients with a new diagnosis of depression who were prescribed SSRIs or tricyclics.⁶ The cohort included 146 095 patients. In comparison with users of tricyclics, users of SSRIs were not at increased risk of suicide or non-fatal self harm. However, in patients aged 18 or less, weak

evidence indicated a higher risk of non-fatal self harm in those prescribed SSRIs.

From a methodological viewpoint, these articles highlight the relevance of combining randomised with observational evidence, taking into account the limitations of both approaches. Randomised controlled trials included selected patient populations followed up for short periods of time: these studies were not designed to identify completed or attempted suicides specifically, and reported data on this outcome variable only in a subgroup of studies.⁴⁻⁵ Additionally, given that a diagnosis of unipolar depression was not required for inclusion in the review, trials with different patient populations were included. Although the procedure of pooling data from hundreds of trials increased the overall numbers, absolute numbers of patients attempting and committing suicide remained very low, leaving the possibility that reporting or not reporting a few cases could have completely changed the overall outcome.⁷ Conversely, the study by Martinez et al analysed a large number of newly depressed patients.⁶ However, the lack of randomisation raises the problem of confounding by indication because doctors might preferentially prescribe SSRIs on safety grounds in patients at risk of suicide. Although authors adjusted statistically for this potential confounder, the possibility that other known or unknown variables might have acted in unpredictable ways cannot be ruled out.

Taking into account these limitations, we can get some useful insights for clinical practice. Firstly, current evidence that indicates no clear relation between SSRIs and suicide,^{4-6 8 9} together with available robust evidence of efficacy of treatment with antidepressant drugs in the pharmacological management of moderate to severe unipolar depression, should encourage doctors to prescribe effective doses of these drugs in such patients. Doctors should additionally be aware that SSRIs, similarly to tricyclics, may induce or worsen suicidal ideation and suicide attempts during the early phases of treatment, possibly because they cause agitation and activation particularly at that time. During these early phases, doctors should plan frequent follow up visits and also consider a possible supporting role for family members and caregivers. Patients should be advised against withdrawing treatment abruptly, given the risk of reactions to discontinuation.¹⁰ Secondly, the strongest evidence applies to moderate to severe depression only and therefore cannot be extrapolated to mild depression.³ Thirdly, these indications apply to adults only, whereas in children and adolescents the balance

Editorials

between benefits and harms seems to be negative, with little evidence of efficacy and increasing evidence of an association between exposure to SSRIs and other antidepressant drugs and emergence of suicidal thought and behaviours.⁶⁻¹¹ This risk, in addition to the lack of data on the long term implications of exposing a developing brain to antidepressant drugs,¹² should discourage the routine prescribing of antidepressant drugs in children and adolescents.

Andrea Cipriani *research fellow in psychiatry*

Corrado Barbui *lecturer in psychiatry*

Department of Medicine and Public Health, Section of Psychiatry and Clinical Psychology, University of Verona, 37134 Verona, Italy (andrea.cipriani@medicina.univr.it)

John R Geddes *professor of epidemiological psychiatry*

Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford OX3 7JX

Competing interests: JG has received research funding and support from Sanofi-Aventis and GlaxoSmithKline and is currently in discussion with several other companies that manufacture SSRIs about collaboration on planned independent trials and systematic reviews.

1 Ustun TB, Ayuso-Mateos JL, Chatterji S, Mathers C, Murray CJ. Global burden of depressive disorders in the year 2000. *Br J Psychiatry* 2004;184:386-92.

- 2 Davies S, Naik PC, Lee AS. Depression, suicide, and the national service framework. *BMJ* 2001;322:1501-2.
- 3 National Institute for Clinical Excellence. *Depression: management of depression in primary and secondary care*. Clinical Guideline 23. London: NICE, 2004. www.nice.org.uk/pdf/CG023quickrefguide.pdf (accessed 6 Feb 2005).
- 4 Fergusson D, Doucette S, Glass KC, Shapiro S, Healy D, Hebert P, et al. Association between suicide attempts and selective serotonin reuptake inhibitors: systematic review of randomised controlled trials. *BMJ* 2005;330:396-9.
- 5 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;330:385-8.
- 6 Martínez C, Rietbrock S, Wise L, Ashby D, Chick J, Moseley J, et al. Antidepressant treatment and the risk of fatal and non-fatal self harm in first episode depression: nested case-control study. *BMJ* 2005;330:389-93.
- 7 Sweeting MJ, Sutton AJ, Lambert PC. What to add to nothing? Use and avoidance of continuity corrections in meta-analysis of sparse data. *Stat Med* 2004;23:1351-75.
- 8 Kahn A, Kahn S, Kolts R, Brown WA. Suicide rates in clinical trials of SSRIs, other antidepressants, and placebo: analysis of FDA reports. *Am J Psychiatry* 2003;160:790-2.
- 9 Jick H, Kaye JA, Jick SS. Antidepressants and the risk of suicidal behaviors. *JAMA* 2004;292:338-43.
- 10 Medawar C. The antidepressant web—marketing depression and making medicines work. *International Journal of Risk & Safety in Medicine* 1997;10:75-126.
- 11 Whittington CJ, Kendall T, Fonagy P, Cottrell D, Cotgrove A, Boddington E. Selective serotonin reuptake inhibitors in childhood depression: systematic review of published versus unpublished data. *Lancet* 2004;363:1341-5.
- 12 Ruchkin V, Martin A. SSRIs and the developing brain. *Lancet* 2005;365:451-3.

Clinical and communication skills

Need to be learnt side by side

Teaching clinical skills to undergraduates focuses on examination, planning treatment, safe prescribing, and procedures such as venepuncture, suturing, and cardiopulmonary resuscitation.¹ Curricula for communication skills aim to develop effective (clear and sensitive) communication with patients, carers, and colleagues. Skills include being able to take a history and share information, particularly explaining procedures and discussing treatment options and their effects.¹ When working with patients and colleagues, communication and clinical skills are practised simultaneously, yet most medical school curriculums teach them separately, albeit in parallel.

The current practice of teaching communication skills separately from clinical skills reflects a reductionist paradigm—by breaking down the complex phenomenon of a consultation to its basic components. This may be helpful at an early stage of learning, but it may limit the coherence needed to ensure that doctors communicate satisfactorily with patients.

Those who teach communication skills have moved on from establishing the importance of their discipline in good clinical care to researching the theoretical base. They now need to return to the clinical workplace to develop further the pragmatics of their teaching. The teaching of clinical skills, by contrast, has enjoyed a time honoured central position in the medical curriculum. The separate development of these two skills has separated them in practice.

In the United Kingdom and United States, the divergence has been compounded by evidence that most complaints are related to poor communication.² This has led to a greater emphasis on communication

skills. The increasing predominance of early community based learning where communication skills are emphasised has also contributed to this dichotomy.

Teaching communication and clinical skills separately does not mirror clinical experience and may lead to unbalanced doctors. Clinicians with sound clinical knowledge may be appraised of the latest research evidence yet unable to translate their skills into effective clinical care.³ Poor communication can often lead to poor health management.^{4,5}

Learning communication and clinical skills side by side would address how important skills for clinical practice can be improved. For example, examination of the abdomen—a clinical skills exercise—requires rapport and clear explanations—a communication exercise. At a more advanced level, evidence based practice integrates patients' values.⁶

A recent challenge in medical education in Europe has been the generally positive imposition of the European Working Time Directive.⁷ The shortened hours of work with limited windows of opportunity for training oblige us to make the most of the time available, and are conducive to integrated models of medical education. The relevant quality agenda has been addressed by Modernising Medical Careers.⁸

An example from postgraduate education of effective side by side learning is the work on developing non-technical skills by using simulated operating theatres for training anaesthetists.⁹ Debriefing, using video review, allows equal emphasis on technical clinical skills and on the social skills for team communication.

Such integrated learning is at an embryonic level in the undergraduate curriculum, but examples include

BMJ 2005;330:374-5