



Antidepressants: not just for depression

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Summary

Antidepressants can be an effective treatment option for a range of disorders other than depression. These include anxiety disorders, eating disorders and premenstrual dysphoric disorder. The efficacy of antidepressants in these disorders is independent of whether there is a mood disorder. However, there is an important, and sometimes superior, role for psychosocial interventions. Caution is needed in prescribing antidepressants if there is a history of bipolar disorder.

Key words: anxiety disorders, eating disorders, premenstrual dysphoric disorder, cognitive behaviour therapy.

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Introduction

In addition to depression, antidepressants may be useful in a range of other disorders. They can be used in the anxiety disorders, and in some eating disorders. The selective serotonin reuptake inhibitors (SSRIs) have been shown to ameliorate the symptoms of premenstrual dysphoric disorder. The tricyclic antidepressants may have a role in the adjunctive management of a range of disorders including chronic pain, headache and enuresis.

Anxiety disorders

Many patients with anxiety disorders do not require drug treatment.

Non-drug treatment

Cognitive behaviour therapy is a highly efficacious treatment for the anxiety disorders. Patients who complete therapy can achieve large reductions in symptom distress and improvements in global functioning. For example, in panic disorder up to 90% of those completing such therapy become panic-free. Exposure-based treatments also have an important role in post-traumatic stress disorder. While pharmacotherapy is associated with high relapse rates following discontinuation, the effect of cognitive behaviour therapy can persist over time. However, some patients are too depressed to participate effectively in cognitive behavioural programs, and comorbid depression is one indicator of poorer outcome. For these patients antidepressant pharmacotherapy may be effective.

Cognitive behaviour therapy can be introduced later as their depression improves.

The question of whether combined cognitive behaviour therapy and antidepressant treatment offers any acute or long-term benefit remains unresolved. In the long term, the inclusion of cognitive behaviour therapy appears to confer some advantage. Hence, current recommendations advise offering cognitive behaviour therapy wherever possible.

Exposure-based programs are the treatment of choice for specific phobias. No drug has established efficacy.

Drug treatment

Although benzodiazepines are effective at reducing the somatic symptoms of anxiety more quickly than antidepressants, they do not result in as great a functional improvement. Antidepressants have an intrinsic anxiolytic action that is not dependent on the presence of comorbid depression or on producing sedation.

Panic

Placebo-controlled trials show that imipramine, clomipramine and the monoamine oxidase inhibitors are efficacious in reducing both the frequency of panic attacks and phobic avoidance.¹ In numerous placebo-controlled trials SSRIs have reduced the frequency and severity of panic attacks, and also improved functioning.

Social anxiety disorder

Monoamine oxidase inhibitors and SSRIs are more effective than placebo, beta blockers and benzodiazepines in the treatment of social anxiety disorder. SSRIs are now considered to be first-line pharmacological treatment and somewhat more than half the patients (or about twice as many as those on placebo) will be much or very much improved.

Obsessive compulsive disorder

In obsessive-compulsive disorder antidepressants only achieve a moderate reduction in symptoms.² Cognitive behaviour therapy has a greater effect. However, approximately 25% of patients refuse this type of treatment and perhaps 25% do not comply with it. In practice, antidepressants and cognitive behaviour therapy are often combined. Only the relatively serotonergic antidepressants, the SSRIs and clomipramine, are effective in treating obsessive compulsive disorder. The benzodiazepines and noradrenergic antidepressants have not been reported to be of benefit.

Generalised anxiety disorder

There are placebo-controlled studies to support the use of certain antidepressants for patients with generalised anxiety disorder. These include imipramine, trazodone (not available in Australia), venlafaxine (a serotonin and noradrenaline reuptake inhibitor) and SSRIs. Importantly, a number of studies have shown antidepressants to be superior to benzodiazepines in relieving the psychic symptoms of anxiety (for example worry, irritability, anxious mood) and equivalent in improving the somatic symptoms. Comorbid depression is particularly common. For these patients early consideration of antidepressant treatment is warranted.

Post-traumatic stress disorder

SSRIs have emerged as first-line pharmacotherapy as they have a more consistent superiority over placebo than monoamine oxidase inhibitors and tricyclics. In addition, several open studies of SSRIs have suggested that they may produce improvements across a broader range of symptoms, including reductions in emotional numbing which is a difficult symptom to treat. As yet, there is little information regarding which patients get the best response, the time course of any response or the optimum dose and duration of treatment.

Using SSRIs in anxiety disorders

SSRIs may have an initial 'activating' effect that can intensify some symptoms of anxiety. It is recommended practice to commence anxious patients on half the minimum tablet strength. The patient remains on this dose for several days to a week until they feel reasonably comfortable; they can then increase to a full tablet. Caution is needed in patients with a history of bipolar disorder as antidepressants can trigger, for example, a manic relapse or rapid cycling.

Many patients will require more than the minimum dose to achieve good control over their symptoms of anxiety and panic. Anxiety disorders differ markedly from depression in the time taken to achieve remission. A recent review reported that after eight weeks of treatment 40–50% of patients have achieved remission, and that this number increases with time.³ There is no evidence to guide the choice of the next antidepressant in the case of non-response or failure to achieve remission.

Eating disorders

Non-drug treatment is the mainstay of management, but antidepressants may have a role in some eating disorders.

Bulimia nervosa

Many antidepressants have been shown in randomised controlled trials to reduce binge eating and purging in patients with bulimia nervosa. Antidepressants also reduce concerns about body weight and shape and reduce symptoms of depression and anxiety.⁴ Tricyclic antidepressants, monoamine oxidase inhibitors, bupropion and SSRIs have all shown efficacy.

There are few controlled follow-up studies. Limited evidence suggests that compared to the treatment of anxiety disorders, there may be better long-term maintenance of gains, providing the initial treatment is continued for long enough (at least six months is recommended). However, it seems that even on continued medication up to one-third of patients may relapse. Open-label studies suggest that changing to a different antidepressant in these cases may produce improvement.⁵

Cognitive behaviour therapy is more effective than antidepressants in bulimia nervosa. The inclusion of cognitive behaviour therapy in a treatment program appears to give some protection against relapse. So far, the evidence is equivocal regarding whether the addition of antidepressants to cognitive behaviour therapy confers any additional benefit in the short term, except to relieve depressive symptoms.⁵

Binge eating disorder

The results of the small number of randomised controlled trials in binge eating disorder suggest that SSRIs may be helpful in reducing binge eating and weight. So far, their long-term effectiveness is unknown.

Anorexia nervosa

In contrast to the bingeing disorders, pharmacotherapy is of no particular value in the treatment of anorexia nervosa. For the severely underweight, nutritional restoration and metabolic stabilisation represent potentially life-saving acute treatment. In the longer term, a holistic, supportive approach is generally recommended, since controlled trials have not shown specific psychotherapy to be superior to non-specific treatment.

Premenstrual dysphoric disorder

Although there has been controversy about the diagnosis, premenstrual dysphoric disorder has been defined as a psychiatric problem. The regular mood disturbance must be differentiated from a primary anxiety or depressive disorder. To establish the diagnosis ask the woman to keep a daily record of her moods and physical symptoms over two successive cycles. Often this in itself will reveal helpful information, for example, identifying exacerbating psychosocial factors that might be amenable to change.

The serotonergic antidepressants (SSRIs and clomipramine), vitamin B₆ (50–100 mg daily), and calcium carbonate (1200 mg daily) given in the luteal phase of the cycle have been shown to be superior to placebo in controlled trials.

SSRIs can reduce the physical and emotional symptoms of premenstrual dysphoric disorder with improvement generally occurring within three cycles. Both continuous dosing (throughout the cycle) and dosing in the luteal phase appear to be effective.⁶ If prescribing the luteal regimen, consider the half-life of the SSRI as discontinuation symptoms may be problematic. Fluoxetine and sertraline are the most studied

SSRIs in premenstrual dysphoric disorder and discontinuation symptoms would not generally be anticipated, especially with fluoxetine given its very long half-life. Doses appear to be within the same range as for the treatment of depression. If a higher dose than the minimum is used and luteal phase dosing is chosen, a short upwards titration is appropriate for SSRIs other than fluoxetine (for example, 50 mg of sertraline for the first three days).⁷

Conclusion

The antidepressants have efficacy in a range of disorders other than depression. In most of these disorders psychological or psychosocial treatments have established efficacy. Antidepressants offer adjunctive treatment for individuals who have a poor response, do not have access to psychological treatments, or who have comorbid depression.

References

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Dr Lampe is a member of the Wyeth Neuroscience Advisory Board.

Self-test questions

The following statements are either true or false (answers on page 107)

3. Antidepressants are not recommended for the treatment of specific phobias.
4. Antidepressants are less efficacious than cognitive behaviour therapy in the treatment of obsessive compulsive disorder.

Book review

Australian Medicines Handbook 2005

Adelaide: Australian Medicines Handbook Pty Ltd; 2005.

909 pages. Price \$135; students \$99; plus postage. Three-year subscription also available.

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Australian prescribers who are unfamiliar with the Australian Medicines Handbook ought to be pleasantly surprised by its many differences from standard medicines guides.

First, the book's structure is noteworthy. Preceding the individual drug monographs are discussions of drug classes, as well as overviews of clinical topics (e.g. heart failure, angina, hypertension) – thus, it is a sort of hybrid of the MIMS and Therapeutic Guidelines books. In many places, and particularly the antibiotics chapter, its recommendations concur with the latter books.

A difference from MIMS is the handbook's independence from the pharmaceutical industry. It contains no advertising and favours generic drug names in the monographs and index (although brand names and manufacturers are listed).

In general, the monographs present carefully distilled drug information at a level of detail ideal for the busy but critically-minded practitioner. They also include 'practice points' and 'patient counselling' sections, which are refreshingly practical and patient-oriented.

The book has an evidence-based flavour. There are frequent references to evidence from trials, with a consistent mindfulness of clinically relevant (rather than intermediate) end points.

Changes from past editions include monographs on newly marketed drugs and some deletions and altered indications. Also new is a long but easily navigable appendix on drug interactions.

The inclusion of more Pharmaceutical Benefits Scheme (PBS) information would make the AMH more useful. Although the reproduction of the PBS schedule *in toto* in the 1998 edition was unnecessarily detailed, I'd like to see the number of available repeats included next to quantity and PBS listing information. Restricted and authority criteria are usually included, but a reproduction of the PBS lipid-lowering drugs statement would be helpful.

Quibbles aside, the 2005 AMH continues the admirable tradition set by its predecessors. It fills a valuable niche as a source of pithy, accessible, independent and evidence-based prescribing information.