Anxiety disorders management

By Stephen Bleakley, MSc, MRPharmS, MCHMP

When deciding how to treat a person with an anxiety disorder, clinicians must consider the duration and severity of symptoms and how the disorder affects the patient’s quality of life. For some patients, a brief intervention using talking therapies will suffice, yet others will require a complex psychological and pharmacological approach. There are advantages and disadvantages to all options and treatment needs to be tailored to the patient — taking into account personal preference, level of engagement and physical and mental comorbidity.

Psychological therapies
There is robust research on the benefits of treating anxiety disorders with psychological therapies, such as cognitive behavioural therapy (CBT), and there is evidence supporting the use of CBT in children and adolescents, and in older adults. CBT is generally considered to be as effective as pharmacological treatment and some studies indicate that relapse rates may be lower with CBT.

CBT focuses on how people’s feelings and thoughts (ie, cognition) drive their actions (ie, behaviours). It is based on the assumption that learning and coping strategies adopted by individuals can affect their ability to adapt to difficult situations. This therapy concentrates on the present, breaks down overwhelming problems into smaller parts and challenges how the patient interprets and reacts to certain situations.

An experienced therapist conducts CBT with individual patients or with groups of patients. Self-help CBT material, such as books or online computer programmes, is also available for patients to use on their own (see accompanying article, p281).

Psychological approaches are the recommended treatment option for patients with separation anxiety disorder, selective mutism or specific phobias. For patients with generalised anxiety disorder (GAD), panic disorder and social anxiety disorder, both psychological and pharmacological treatments are recommended.

Antidepressants
Antidepressants are recommended treatment options for GAD, panic disorder and social anxiety disorder. Choice of antidepressant depends on the type of disorder, supporting evidence and the UK marketing authorisation of the

Some anxiety disorders, such as selective mutism and specific phobias, are best treated using non-pharmacological interventions, eg, cognitive behavioural therapy. Other disorders require a combination of pharmacological treatment and psychological support.

Antidepressants, specifically those that enhance the level of serotonin in the brain, are recommended treatment options in generalised anxiety disorder, panic disorder and social anxiety disorder. Second-line options include pregabalin and benzodiazepines.

National guidelines
The National Institute for Health and Care Excellence has produced guidelines on GAD and panic disorder (with or without agoraphobia) and social anxiety disorder (see Box 1, p287).

The British Association for Psychopharmacology is currently updating its 2005 guideline on anxiety disorders and the revision is expected to be published early in 2014. International guidelines are also available from the World Federation of Societies of Biological Psychiatry.

Antidepressants
Antidepressants are recommended treatment options for GAD, panic disorder and social anxiety disorder. Choice of antidepressant depends on the type of disorder, supporting evidence and the UK marketing authorisation of the
medication. Antidepressants with serotonin-enhancing properties are preferred and selective serotonin reuptake inhibitors (SSRIs) should be tried first. SSRIs inhibit the presynaptic reuptake of serotonin — increasing serotonin transmission. Common adverse effects include nausea, vomiting, diarrhoea (usually subsides within a few weeks), insomnia and sexual dysfunction (this can persist).

The serotonin and noradrenaline reuptake inhibitors (SNRIs) venlafaxine and duloxetine inhibit the presynaptic reuptake of both serotonin and noradrenaline. Adverse effects are similar to those of SSRIs, and sweating, increases in blood pressure and palpitations are also occasionally reported.6

With antidepressant therapy, worsening of anxiety symptoms can occur at the beginning of treatment and patients should be monitored closely for adverse effects and discontinuation of treatment. Titrating the dose slowly, starting at half the usual dose for the treatment of depression, is recommended; however, the final effective dose will often exceed the dose used for depression. The SSRIs and SNRIs have also been associated with an increased risk of bleeding, rare reports of suicidal ideation in people under 30 years and discontinuation symptoms (eg, flu-like symptoms, insomnia and irritability).9

NICE recommends that a tricyclic antidepressant, either imipramine or clomipramine, can be used for panic disorder if an SSRI has not been effective.7 Tolerability issues, such as sedation, hypotension and constipation, and the risk of cardiac toxicity in overdose may limit the use of these medicines for some patients.

For social anxiety disorders that have failed to respond to an SSRI or an SNRI, phenelzine, a monoamine-oxidase inhibitor, or moclobemide, a reversible monoamine-oxidase inhibitor, may be considered. Foods containing tyramine must be avoided when taking phenelzine to prevent potentially dangerous increases in blood pressure. Although agomelatine is not currently licensed or included in NICE guidance, randomised controlled trials investigating its use in GAD have been positive.10 Mirtazapine has been shown to have a positive effect on GAD in one small pilot study.11

Response to antidepressants usually occurs within six weeks. If effective, they should be continued for at least a month. If the patient chooses pharmacological therapy, consider a serotonin and noradrenaline reuptake inhibitor (SNRI; eg, venlafaxine or duloxetine) drug; however, note that it does not currently have UK marketing authorisation for this indication. If sertraline is ineffective, consider another SSRI or a serotonin and noradrenaline reuptake inhibitor (SNRI; eg, venlafaxine or duloxetine) drug. If sertraline is ineffective, consider another SSRI or a serotonin and noradrenaline reuptake inhibitor (SNRI; eg, venlafaxine or duloxetine).

Pregabalin

Although pregabalin is a structural analogue of gamma-aminobutyric acid (GABA), it does not have an immediate effect on GABA receptors. Instead, it binds to voltage-gated calcium channels, changing their conformation in a way that is thought to reduce excitatory neurotransmission.

There is strong evidence to support the use of pregabalin in the acute treatment of GAD and to prevent relapse.12 There is evidence of efficacy in young patients and the elderly, and it is thought that pregabalin can also enhance the effects of SSRIs or SNRIs.12 NICE has recommended pregabalin as a treatment option for GAD when SSRIs and SNRIs have not been tolerated.7 The findings of some studies support the use of pregabalin in social anxiety disorder;14 however, it is not licensed or recommended by NICE for this indication. Pregabalin acts quickly — often within a few days — and is generally well tolerated across the recommended daily dose range (150–600mg). The two most frequently reported adverse effects are dizziness and somnolence.5 Pregabalin is almost completely excreted unchanged, meaning drug interactions involving cytochrome P450 isoenzymes are not an issue; however, doses need to be adjusted for patients with renal impairment.

There have been reports of pregabalin abuse — usually among those with a previous history of substance...

---

**Box 1: Summary of NICE guidance**

The National Institute for Health and Care Excellence has produced guidance on the management of three of the anxiety disorders: generalised anxiety disorder (GAD), panic disorder (with or without agoraphobia) and social anxiety disorder.

**Generalised anxiety disorder**

Recommendations for the treatment of patients with GAD:

- Consider offering self-help material and psychoeducation as first-line interventions.
- For those who do not respond to first-line interventions, offer high-intensity psychotherapy, such as applied relaxation or cognitive behavioural therapy (CBT), or offer pharmacological therapy according to patient preference.
- If the decision to start pharmacological therapy has been made, consider using selective serotonin reuptake inhibitors (SSRIs) first line.
- Consider offering sertraline first because it is the most cost-effective drug; however, note that it does not currently have UK marketing authorisation for this indication.
- If sertraline is ineffective, consider another SSRI or a serotonin and noradrenaline reuptake inhibitor (SNRI; eg, venlafaxine or duloxetine).
- Consider pregabalin if the person cannot tolerate SSRIs or SNRIs.
- Do not offer benzodiazepines (except as a short-term measure in crisis).

**Panic disorder (with or without agoraphobia)**

Recommendations for the treatment of patients with panic disorder:

- Choice of treatment should be guided by patient preference and what they have previously responded to.
- An SSRI licensed for panic disorder (eg, sertraline, citalopram or escitalopram) should be considered for first-line pharmacological treatment.
- If an SSRI is ineffective or not suitable, clomipramine or imipramine may be considered.
- Benzodiazepines are associated with poorer long-term outcomes and should not be prescribed.
- Sedating antipsychotics or antihistamines should not be prescribed.

**Social anxiety disorder**

Recommendations for the treatment of patients with social anxiety disorder:

- Offer individual CBT to adults. If this is declined consider providing the patient with self-help material on CBT techniques.
- For patients who do not wish to engage in CBT, discuss their reasons and address any concerns.
- If the patient chooses pharmacological therapy, consider an SSRI (eg, sertraline or escitalopram) and monitor closely for adverse effects.
- For children or adolescents, offer individual or group-based CBT. Consider involving the parents or carers in group CBT sessions.
misuse — and this may be related to the occasional adverse effect of euphoria that is experienced by 1–10% of users; however, the abuse potential of pregabalin is considered to be much lower than that of benzodiazepines.

Benzodiazepines

Benzodiazepines have been in use for over 50 years and are still considered to be effective in the treatment of persistent and severe anxiety symptoms. Although there is evidence to support the use of benzodiazepines (mainly diazepam and clonazepam) in GAD, panic disorder and social anxiety disorder, sedation, falls, dependence and abuse can limit their usefulness. Benzodiazepines should be used for the shortest period possible (maximum of four weeks) at the lowest possible dose for patients in crisis. Although NICE suggests that benzodiazepines should not be prescribed for panic disorder or social anxiety disorder, other national and international guidelines recommend that benzodiazepines are used for patients whose symptoms are not responsive to other treatments.

Long-term use of benzodiazepines should be avoided, but may be appropriate for people with persistent, treatment-resistant and crippling anxiety.

For patients with a history of substance misuse, or previous benzodiazepine abuse, strict treatment plans with close monitoring are required. Up to one third of patients prescribed benzodiazepines will continue them long-term — around half of whom may develop physiological dependence. Withdrawal from benzodiazepines should be managed carefully (see Box 2).

Other options

Buspirone Although the exact mechanism of action of buspirone is not fully known, it is thought to be a serotonin (5HT1A) receptor partial agonist. It is licensed for short-term use in anxiety and there is some evidence supporting its use for when the anxiety symptoms of GAD first appear. A Cochrane review found that buspirone was better than placebo in short-term studies (4–12 weeks), but less effective or tolerable than benzodiazepines. Taking buspirone 10mg three times a day for at least four weeks is required for it to have a full effect.

Quetiapine Quetiapine has been shown to be of similar efficacy to antidepressants in reducing the symptoms of GAD; however, adverse effects, such as sedation and weight gain, are common and dropout rates are high. Plans for NICE to conduct a technology appraisal on quetiapine in GAD have been suspended. There is some evidence to support the use of other antipsychotics in post-traumatic stress disorder and obsessive compulsive disorder.

Beta-blockers Although evidence is lacking, propranolol and other beta-blockers are occasionally used to manage the physical symptoms of anxiety, such as tremor, palpitations, sweating and shortness of breath. People with anxiety often experience dizziness or postural hypotension: these symptoms can be exacerbated by beta-blockers.

Hydroxyzine Hydroxyzine has been found to be more effective at treating GAD than placebo; however, few studies have compared hydroxyzine with other treatment options and it is not recommended.

Comparative studies

A number of multiple-treatment meta-analysis studies of psychotropic research have been published in recent years. These studies attempt to rank, in terms of efficacy and tolerability, the medicines used in a condition by analysing direct and indirect literature.

One such review was published in 2011: David Baldwin and colleagues compared nine of the most commonly used medicines in GAD. Fluoxetine was rated first for both response and remission, and sertraline came first for tolerability.
Sub-analysis of UK-licensed medicines for GAD rated duloxetine first for response, escitalopram first for remission and pregabalin first for tolerability.50

References
11 Bazin S. Psychotropic drug directory. Ware, UK: Lloyd-Reinhold Communications; 2014.

Boost your continuing professional development by completing our Lifelong Learning modules at www.clinicalpharmacist.com

Anxiety disorders

Lifelong Learning questions are available to complete in an online module on the Clinical Pharmacist section of PJ Online — accessible via www.clinicalpharmacist.com.

To complete the module, you will need to log in to the site. If you are a new visitor, it is simple to register as a user (free to all Royal Pharmaceutical Society members).

Questions

This month’s Lifelong Learning questions are based on the CLINICAL FOCUS articles on anxiety disorders, which were commissioned from an independent author. The information in the Box (below) is there to help you identify knowledge gaps and undertake continuing professional development. This online module will close on 6 March 2014.

Answers from the October module

Idiopathic pulmonary fibrosis

1 (a) T, (b) T, (c) F, (d) F, (e) F
2 (a) F, (b) T, (c) F, (d) T, (e) F
3 (a) T, (b) F, (c) T, (d) T, (e) T
4 (a) T, (b) F, (c) T, (d) F, (e) T
5 (a) F, (b) T, (c) F, (d) F, (e) T
6 (a) T, (b) T, (c) T, (d) F, (e) F
7 (a) T, (b) F, (c) T, (d) T, (e) F
8 (a) T, (b) T, (c) T, (d) F, (e) T
9 (a) F, (b) F, (c) T, (d) F, (e) F
10 (a) T, (b) F, (c) F, (d) F, (e) T

Answers

When you have completed the online module, your answers will be submitted for marking and Clinical Pharmacist will send you a certificate and your results by email within two weeks of the module closing.

How to undertake continuing professional development

Our CLINICAL FOCUS articles and the online Lifelong Learning modules can help you plan your CPD and record the benefits of the activity at www.uptodate.org.uk.

Reflect on your gaps in knowledge

What is anxiety and how can it affect quality of life?
How is anxiety diagnosed?
What is cognitive behavioural therapy and how effective is it for treating anxiety?
What medicines are used in the treatment of anxiety?

Act to enhance your practice

Read the CLINICAL FOCUS articles in this issue (pp281–9)

Test your knowledge by completing the questions at www.clinicalpharmacist.com

Evaluate the activity

What have you learnt?
How has it added value to your practice?
What will you do now and how will this be achieved?

The questions in this Lifelong Learning module have been appraised by an independent reviewer for quality assurance.

Consider making this activity one of your nine CPD entries this year