Assessing and treating mixed depression and anxiety

How can clinicians make sense of patients experiencing both depression and anxiety, and decide on treatment? This article reviews the overlap between depression and the various anxiety disorders and details the various pharmacological and psychological therapeutic options.

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The co-occurrence of depression and anxiety is common in clinical practice. The Australian National Survey of Mental Health and Well-Being found that in the 12 months prior to interview, 5.8% of the adult population had major depression and 9.7% an anxiety disorder.[1] However, depression alone accounted for only 1.4% of the population and an anxiety disorder alone only 2.9%. Significantly, over 3% reported mixed anxiety and depression. These figures indicate that such mixed presentations are more common than ‘pure’ presentations of anxiety or depression – a fact well known to experienced clinicians.

Why does it matter whether depressed patients are anxious, or vice versa? The major reason is that such comorbidity is generally associated with more severe illness. Patients with comorbid depression and anxiety (e.g. generalised anxiety disorder, panic disorder, etc) are less treatment responsive, are more functionally impaired and disabled, have a higher suicide risk, and are slower to respond to treatment.[2]

The increased disabling effect can be seen, for example, in data from the Australian National Survey. The average ‘days out of role’ in the prior 12 months due to the combination of anxiety and depression was 3.6, compared with 2.1 days for anxiety alone and 2.7 for depression.[1]

How to approach the mixed presentation

We recommend that the most clinically useful approach to deciding on treatment for patients with depression and anxiety is to determine which disorder was the first to appear. For most patients with a mixed presentation, this is a helpful means of making sense of their complexity and enables a clear point of intervention.

There is little doubt, however, that some

IN SUMMARY

- **Comorbidity of depression and anxiety is generally associated with more severe illness.**
- **The most clinically useful approach to deciding on treatment for patients with mixed depression and anxiety is to determine which disorder was the first to appear.**
- **If the depression was the first condition to appear, or was subsequent but is marked or severe, treat the depression. Once the depression is adequately treated, address the anxiety disorder.**
- **If the anxiety disorder was the initial presentation and the depression is not severe, the first step should be treatment of the anxiety disorder.**
- **Treatment may involve pharmacological therapy, cognitive behavioural therapy, or both.**
- **It is a fallacy that depressed patients with anxiety symptoms necessarily require sedative antidepressants such as mirtazepine, nefazodone or the tricyclics.**
- **The two main cognitive vulnerabilities that put individuals at heightened risk of depression are interpersonal sensitivity and too much focus on achievement to feel worthwhile.**

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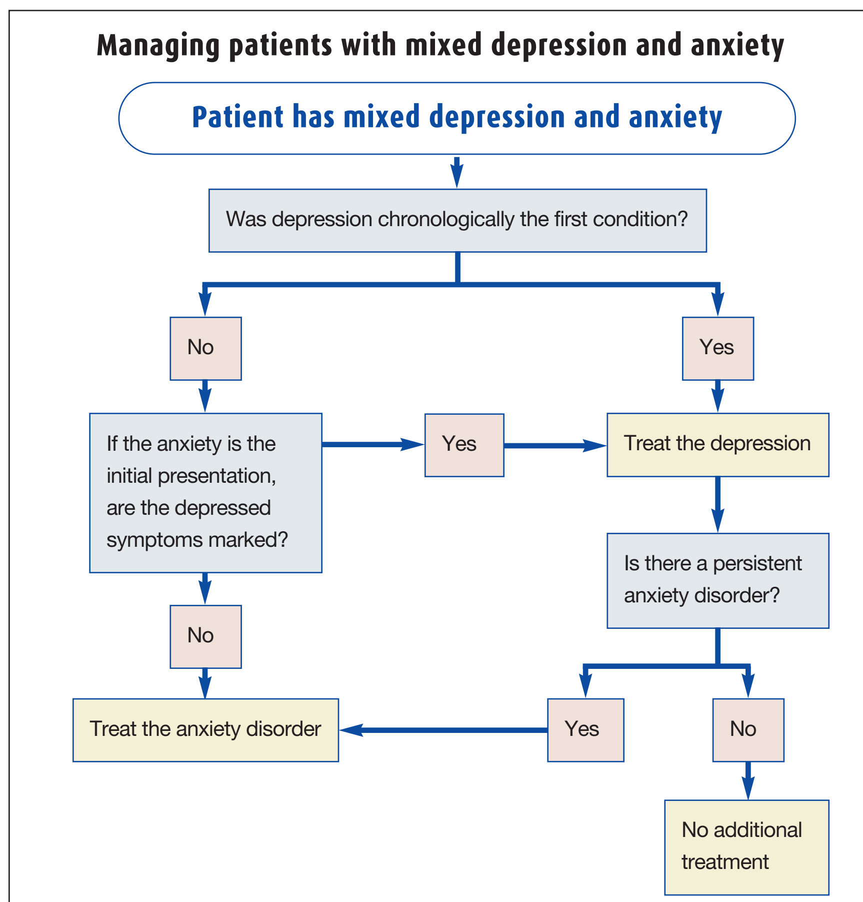

patients present with the concurrent onset of both depression and anxiety. For such patients the terms 'generalised distress syndrome' or 'generalised neurotic syndrome' have been applied. These terms are not recognised in the American DSM-IV or the WHO ICD-10 diagnostic classification systems. For patients who have anxiety and depression not sufficiently severe to fulfil the criteria for either a major depressive illness or a specific anxiety syndrome, the term 'mixed anxiety depression' has been coined. This controversial entity probably presents more commonly in general practice than in the psychiatric setting. At present, the diagnosis of 'mixed anxiety depression' has not been incorporated in the DSM system, though it is in the ICD-10 classification.

Clinically, anxiety symptoms may be the main manifestation of depression, and vice versa. It is therefore critical to enquire always about symptoms of both conditions. For example, anxiety presenting for the first time in an older patient may be indicative of an underlying depressive illness alone.

Principles of management

The principles of management are outlined in the flowchart above.

If the depression was the first condition to appear, the presentation should be treated as if it is a depressive illness. Furthermore, if the depression is clearly subsequent but is marked or severe then it should still be treated first. (Empirically it has been found difficult to treat anxiety disorders satisfactorily if there are significant levels of depression.) Once the depression is adequately treated then the anxiety disorder needs to be addressed in its own right.

If the anxiety disorder is the initial presentation and the depression is not severe, the first step should be treatment of the anxiety disorder. Usually the consequent symptoms or disorders resolve when the initial disorder is treated.

If the picture is one of 'mixed anxiety depression', the initial treatment is determined by the most severe symptoms (e.g. treat the depression first if that is most prominent).

Depression

For a diagnosis of major depression, at least five of the following symptoms must be present for at least two weeks (at least one of the first two symptoms must be included):

- depressed mood
- loss of interest or pleasure
- significant loss or gain of appetite or weight
- insomnia or hypersomnia
- psychomotor agitation or retardation
- fatigue or loss of energy
- feelings of worthlessness or excessive guilt
- impaired thinking or concentration, indecisiveness
- suicidal thoughts or thoughts of death.

Pharmacological therapy

As detailed guidelines on the use of antidepressant medications are available elsewhere (e.g. the *Therapeutic guidelines: psychotropic*[3]), these will not be further discussed here. Some general comments on the treatment of depression with anxiety symptoms are, however, necessary.

First, although a small proportion of patients who are treated with antidepressants such as the selective serotonin reuptake inhibitors (SSRIs) or venlafaxine (Efexor) develop anxiety as an adverse effect, the majority of patients experience a reduction of anxiety symptoms in parallel with the antidepressant response (see Case A on page 41). It is a fallacy that depressed patients with anxiety symptoms

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necessarily require sedative antidepressants such as mirtazapine (Avanza, Mirtazon, Remeron), nefazodone (Serzone) or the tricyclics.

Second, despite claims to the contrary, there is no evidence that any particular antidepressant (such as a particular SSRI) is more effective than any other for treating depression with comorbid anxiety or panic. The only antidepressant that should perhaps be avoided in depressed patients with concurrent anxiety disorder is reboxetine (Edronax), which appears to produce relatively high rates of anxiety and insomnia.

Cognitive behavioural therapy

Cognitive behavioural therapy is based on the idea that depression is determined, at least in part, by the individual's negative thoughts, assumptions and underlying attitudes. Cognitions such as 'what's the point' or 'there is no hope for me' may serve to trigger and/or maintain depressed affect. Such negative thoughts generally prevent individuals from solving problems and regaining a sense of control.

There are two main cognitive vulnerabilities that make individuals at heightened risk of depression. The first is interpersonal sensitivity or the tendency to become excessively hurt by perceived or real rejection (for example, someone with this trait might notice that his or her partner is irritable on returning home from work, and take this personally despite reassurances to the contrary). The second is too much focus on achievement to feel worthwhile. Clearly, this places individuals at risk of depression if they are thwarted from achieving their goals, lose their job and so on.

The immediate goal of cognitive behavioural therapy is symptom relief through modifying negative thoughts. The longer term goal is to modify unhelpful underlying assumptions and solve problems in daily living or relationships, which in turn aims to prevent further episodes of depression.

Generalised anxiety disorder

The diagnostic criteria for generalised anxiety disorder include excessive anxiety and worry about a number of events or activities for a period of six months or longer. The anxiety and worry are associated with three or more of the following:

- restlessness or feeling 'keyed up' or on edge
- being easily fatigued
- difficulty concentrating or mind going blank
- irritability
- muscle tension
- sleep disturbance.

Case B, on this page, is a presentation of generalised anxiety disorder with secondary depression.

Pharmacological therapy

In general, pharmacological therapies play little role in the management of generalised anxiety disorder. Some antidepressants (such as venlafaxine and paroxetine) have received marketing approval for the treatment of this condition, but the clinical effect is modest.

Benzodiazepines are most useful for acute anxiety (up to one month) but become less effective with time. Daily use of benzodiazepines for more than one to two months is likely to lead to physical and/or psychological dependence.

Buspirone (Buspar) is a nonbenzodiazepine anxiolytic which does not induce dependence. Its effectiveness is, however, limited (and it is not PBS listed).

Cognitive behavioural therapy

Individuals with generalised anxiety disorder are fearful and view themselves and situations around them as threatening.

Case A. Depression with secondary anxiety

Mr E, a businessman in his early 60s, presented with anxiety and insomnia in the context of business difficulties. Although he had some perfectionistic traits and tended to be a worrier, he had never previously suffered from severe anxiety and had been very competent and successful in his career. On closer questioning, it was apparent that he was now reluctant to go to work, although he normally enjoyed this, thriving on the 'cut and thrust' of the commercial world. He had lost interest in his normal pleasures, such as golf and holidays. He had become forgetful and his concentration was impaired. He admitted feeling unhappy and depressed, though he had no suicidal thoughts.

Treatment with an SSRI antidepressant (coupled with counselling concerning his work situation) led to successful regulation of both his depressive and anxiety symptoms.

Case B. Generalised anxiety disorder with secondary depression

Mr K, a builder in his late 20s, presented with reactive depression in the context of stresses associated with his work. On further questioning, it became apparent that he had a long history of performance anxiety, perfectionism, obsessionality, fear of failure and hypersensitivity to criticism and rejection. He had experienced generalised anxiety and low self-esteem since adolescence and relied on praise from others to feel good about himself. When unable to deal with the stresses at work, he described feeling worthless, helpless and hopeless and had started abusing alcohol in an attempt to block out his emotions. Usually quiet and placid, he had become irritable and aggressive towards others.

He was treated with cognitive behavioural therapy focusing on the anxiety disorder.

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Case C. Social phobia with secondary depression

Mr L was an overseas student in his early 20s who presented with depression consequent upon marked social phobia. Ever since his adolescence he had been markedly sensitive to being scrutinised by others. When he moved from overseas he became exquisitely sensitive to others looking at him, particularly in tutorials. As he continued in his studies he became less confident and began to become depressed and anxious. He found it difficult to concentrate, became hopeless about his future, and at times was preoccupied by suicidal thoughts.

After initial treatment with a series of antidepressants was unsuccessful, he received cognitive behavioural therapy, responding well to that.

Case D. Depression secondary to agoraphobia

Mrs S, a secretary in her late 40s, presented with agoraphobia with panic attacks and depression. She sought professional help after experiencing difficulty breathing when confronted with situations where escape routes were not readily available, the main problem areas being lifts, airplanes, tunnels, crowded places and public transport. She also expressed concerns about possible cardiac problems, fearing that she was going to die (all her medical investigations were normal). She had become frightened of leaving home and was unable to work.

She described being unhappy in her marriage and feeling trapped, describing her husband as domineering and unsupportive. Furthermore, her children had left home and were getting on with their own lives. She had lost interest in her usual activities and was becoming increasingly isolated, with feelings of inadequacy and hopelessness.

Her panic and depression responded well to cognitive behavioural therapy that was focused on the agoraphobia.

They are forever watchful for signs of danger and constantly anticipate that something bad is going to happen.

Negative cognitions revolve around control, responsibility, predictability and safety. Individuals select out features in situations that confirm their perceptions of threat and danger. For example, someone with generalised anxiety disorder might not hear from a member of the family for a couple of days and become convinced that there is something wrong. Cognitive behavioural therapy involves checking out the evidence for such beliefs and developing more realistic appraisal mechanisms.

Panic disorder

Panic disorder is recurrent panic attacks characterised by:

- palpitations
- sweating
- trembling
- dyspnoea
- choking sensation
- chest pain or discomfort
- nausea
- dizziness, light headedness
- derealisation
- fear of going crazy or dying
- tingling
- hot flushes.

Pharmacological therapy

All the SSRIs have been shown to be antipanic agents, and appear to be more acceptable than the tricyclics for this disorder. Alprazolam is also indicated for this condition, although withdrawal from this benzodiazepine is often difficult.

For illness not responding to other medications, the older monoamine oxidase inhibitors (MAOIs), such as phenelzine (Nardil) or tranylcypromine (Parnate), may be helpful. They do, however, have a higher risk of serious and even life threatening side effects.

Cognitive behavioural therapy

Panic attacks result from the catastrophic interpretation of bodily sensations such as hyperventilation, palpitations, breathlessness and dizziness. Individuals with panic disorder become hypervigilant and perceive these sensations as signs of immediate physical or mental disaster leading to complete loss of control. For example, difficulty swallowing may be regarded as evidence of a choking attack; palpitations may be seen as indicative of a heart attack.

In this context, cognitive behavioural therapy involves a combination of controlled breathing, progressive muscular relaxation, cognitive restructuring and exposure. It also involves identifying the sequence of events that trigger the panic attacks, which may include particular thoughts, images, bodily feelings or situations. The interpretation of these sensations is then examined and modified. Some individuals only believe that another interpretation applies if it can be shown in behavioural experiments, such as voluntary hyperventilation. Avoidance of particular situations may also reinforce negative interpretations, so cognitive behavioural therapy encourages individuals to approach situations that they may be been avoiding.

Social phobia and agoraphobia

Phobias are marked fears of situations or objects that are recognised by the sufferer as unreasonable or excessive and which interfere with normal function by the resulting discomfort or by measures taken to avoid the precipitating factors.

Social phobia is a marked and persistent

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fear of social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others (see Case C on page 42). The individual fears that he or she will act in a way that will be humiliating or embarrassing.

Agoraphobia is the fear and avoidance of being in places or situations from which escape might be difficult or embarrassing, or in which help might not be available in the event of suddenly developing a symptom that could be incapacitating or embarrassing (e.g. dizziness, derealisation, loss of bladder or bowel control). As a result of this fear, the person either restricts travel or needs a companion when away from home, or else endures agoraphobic situations despite intense anxiety (see Case D on page 42).

Pharmacological therapy

The major medications for social phobia are the SSRIs and the MAOIs – both the older agents (tranylcypromine and phenelzine) and moclobemide. In general, the clinical benefit from such medications is only moderate at best.

There are no specific medications for agoraphobia. All the treatments described for panic disorder can be used for agoraphobia associated with panic attacks.

Cognitive behavioural therapy

The cognitive model views social phobia in terms of pervasive distressing thoughts related to the fear of being evaluated negatively or rejected. This generally leads to profound feelings of shame or embarrassment.

In addition to modifying beliefs, cognitive behavioural therapy involves graduated exposure to social situations that the individual has been avoiding because of high anxiety. Other techniques used to manage the anxiety include relaxation, distraction, role playing and rehearsal of typical situations. For maximum improvement, group cognitive behavioural therapy is recommended for people with social phobia.

All the elements described for panic disorder may be applied to agoraphobia. The symptoms of agoraphobia generally centre on a marked avoidance of situations that individuals fear they will have difficulty escaping from. The fear of feeling anxious and subsequently being trapped is paramount. The further individuals with agoraphobia move away from their safe place, the more anxious they become.

Cognitive behavioural therapy for agoraphobia involves a combination of cognitive restructuring, graded exposure and behavioural experiments. Facing situations that are feared is fundamental to breaking the vicious cycle of anticipatory anxiety and avoidance. As with social phobia, group cognitive behavioural therapy is often beneficial.

Obsessive compulsive disorder

Obsessions are recurrent and persistent intrusive ideas, thoughts, impulses or images that are usually resisted by the patient and are recognised as the product of his or her own mind and not imposed from without.

Compulsions are repetitive, stereotyped behaviours in response to an obsession, to prevent discomfort or some dreaded event with which the rituals are not connected in a realistic way. The person generally recognises that his or her behaviour is excessive or unreasonable.

Pharmacological therapy

All of the SSRIs and the tricyclic clomipramine have been found to be effective for obsessive compulsive disorder. The anti-obsessive compulsive disorder effect is slower than the usual antidepressant action, with a delay of 8 to 12 weeks necessary before significant benefit is seen. Additionally, the dosage required to treat obsessive compulsive disorder is often higher than that required for depression – for example, 60 to 80 mg of fluoxetine may be necessary to obtain an anti-obsessional effect, unlike depression where 20 mg is usually sufficient.

Cognitive behavioural therapy

Recurrent obsessive thoughts or images are generally distressing to patients. As a result, they may feel compelled to repeatedly perform certain compulsive rituals to neutralise the thoughts (e.g. excessive checking, ritualistic counting, hand washing).

Treatment involves deliberate and direct exposure to the feared thoughts and situations, and prevention (if relevant) of the compulsive behaviours and rituals. Therapy also includes habituation training, which involves getting the individuals used to the upsetting thoughts without their doing anything about them. Techniques include repeating the intrusive thoughts several times, writing them down repeatedly or using a tape-recorded loop of the thoughts in the individual's own voice. Another strategy involves 'thought stopping', which aims to consciously dismiss intrusive thoughts and thereby reduce their duration and intensity.

Conclusion

Comorbid depression and anxiety is common in clinical practice and leads to greater levels of disability. The principles of management outlined in this article should enable rational decision making about treatment choices, be they pharmacological, psychological or both. MT

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Further reading

1. Tanner S, Ball J. Beating the blues: a self-help approach to overcoming depression. Sydney: Doubleday, 1989.

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