deNovo Medica

Leader in digital CPD for Southern African healthcare professionals

Anxiety: Module 2

Treating anxiety disorders in primary care

Expert

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Introduction

It is important to note that most patients do not visit their general practitioner specifically for the treatment of anxiety. Patients tend to present with physical complaints, generally unaware of the link between these symptoms and their anxiety or stress levels.

Anxiety in primary care is so common that it is frequently missed. As a result, less than 50% of patients with general anxiety disorder (GAD) are diagnosed, and only one-third receive treatment for their condition. It is not essential to diagnose anxiety at first visit; but be aware that it may be a probable cause of physical symptoms or sleeplessness, and watch and wait for it to manifest.

Anxiety and depression are closely related, with 60-80% of GAD patients developing major depression requiring treatment. Anxiety and attention deficit hyperactivity disorder (ADHD) also frequently occur together.

KEY MESSAGES

- Patients are generally unaware of the link between their physical symptoms and their anxiety or stress levels
- Assessment of severity and duration of symptoms is necessary when deciding on evidence-based pharmacological or psychological treatments
- An individualised biopsychosocial approach is the first principle of treatment
- Exercise has an important positive role to play in the treatment of anxiety.

Neurobiology of anxiety

The major areas of the brain involved in the anxiety state are the amygdala, ventromedial frontal cortex and the anterior cingulate cortex.[1] The microstructure of the fibres linking the prefrontal cortex (which mitigates the anxiety state) and the amygdala (which provokes the anxiety state) differs between individuals. Imaging studies[2] using positron emission tomography (PET) have shown weaker linkage fibre pathways in persons who are trait-anxious. These effects occur in the right hemisphere with a specific microstructure being associated with an anxious personality, and a different structure being associated with an effective emotion-regulation style of anxiety behaviour. This may explain why cognitive behavioural therapy (CBT) does not work in all patients.

Anxiety in primary care is so common that it is frequently missed

What are the concerns about psychotropic medication?

Patients with anxiety and stress or panic disorder generally fear loss of control. So, although they want help, taking and continuing with medication is problematic. "In my view, with anxiety or panic disorder patients, pharmacological treatment approaches need to go slowly," advises Professor Oosthuizen. It is important for the patient to take time and accept the value thereof. The difficulty associated with it can be further exacerbated by some health professionals and commentators who consider pharmacological intervention as merely symptomatic treatment and not a holistic treatment.

At the outset, the severity and duration of symptoms, with their associated distress and impairment, must be assessed when deciding which patients should be offered pharmacological or psychological

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treatment. Co-existing depression or other potential comorbid disorders must be considered, and the patient thoroughly assessed in respect of the presence of physical illness, current concomitant medication and a history of good or poor response to previous treatment. Professor Oosthuizen stresses that 80-90% of patients with GAD and panic disorder should be treated at primary care level.

"80-90% of patients with GAD and panic disorder should be treated at primary care level"
Professor Oosthuizen

Treatment recommendations

The first principle when treating anxiety is to apply a biopsychosocial approach, as the evidence supports the combination of psychotherapy and medication in the context of the individual's own thoughts, feelings and history (Figure 1). When selecting treatment options, Professor Oosthuizen emphasises that it is vital to tailor a package of interventions for each individual based also on the patient's preference.

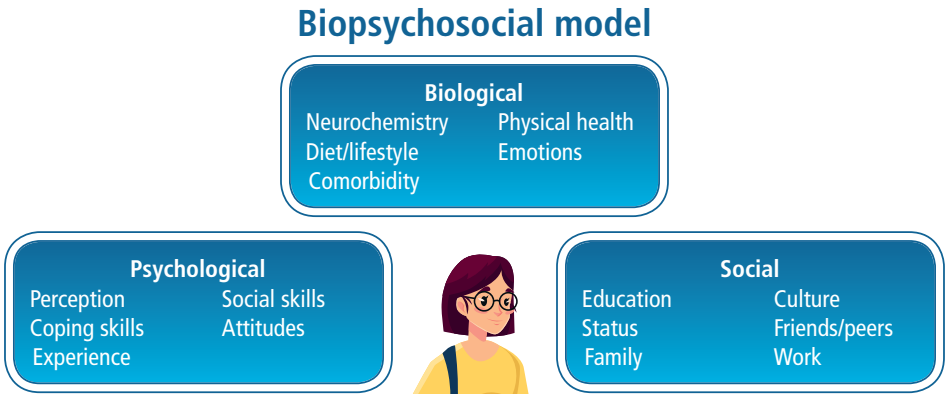

Figure 1. Biopsychosocial model

Evidence-based psychotherapy

The most positive evidence for the use of psychotherapy in anxiety supports the use of manual-based CBT, perhaps because this intervention is measurable and has therefore been evaluated more frequently than psychodynamic therapy, for example. CBT should be part of the treatment strategy in anxiety management.

A recent review of the value of psychodynamic therapy has noted that this approach can be used as a second-line strategy; it has been shown to be efficacious in major depressive disorder (MDD) and social anxiety disorder, and is possibly efficacious in panic disorder and GAD.[3] There is insufficient evidence for a variety of non-therapist-supported techniques over the internet.

When electing not to use CBT, the possible medicolegal complications must be assessed. Clinical notes need to address why this avenue was not selected, as these may be needed as substantiation in case of possible future litigation.

Evidence-based pharmacotherapy

GAD

There is evidence for the use of selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), clomipramine and pregabalin in the treatment of GAD (Table 1).[4]

It is important to note that antidepressants take weeks to become effective. For most antidepressants the dose-response curve is quite flat, so it is essential to 'start low and go slow'. Venlafaxine is an exception as it has an ascending dose-response curve and a more rapid onset of action.

Of importance is the new approach to antidepressant dosage levels, viz. that the dose which gets the patient well *is* the maintenance dose, and should not be tapered-off. Therapy should be maintained and continued for 6-12 months after remission, or even longer. Thereafter, a slow tapering can be introduced until the end of therapy. Fluoxetine, with its longer half-life of five days, can be useful as a switch towards the end of tapering off an SSRI. Agents with a longer half-life can help to ease the withdrawal from SSRIs.

Table 1. Agents with evidence of benefit in GAD therapy[4]

• SSRIs	• Clomipramine
• SNRIs	• Pregabalin

"It is vital to tailor a package of interventions for each individual based also on the patient's preference"
Professor Oosthuizen

The role of combination therapy in anxiety disorder treatment

The evidence points to a better resolution of anxiety disorders when a combination of therapies is used after a non-responsive effect to one therapy used for 4-6 weeks. There are many options for switching within a class, particularly the SSRIs, as each medication has a different molecular structure and pharmacokinetic effect.

Therapeutic options include switching to an SNRI or to other agents with anxiolytic effects such as pregabalin, starting low with 25mg at night. Continue at this dose for 3-5 days before increasing the medication.

When considering second-generation antipsychotics such as quetiapine for off-label use in anxiety disorders, medico-legal issues must be considered.

In summary, for treatment of GAD the clinician can select from the antidepressants, pregabalin, benzodiazepines (used correctly and preferably short term) and atypical antipsychotics.

Table 2 provides a useful stepwise plan for alternative drug treatment.[4,5] The Maudsley prescribing guidelines advise the use of SSRIs, SNRIs and pregabalin as first-line therapy for anxiety disorders (Table 3).[6] Table 4 is a usage table based on the personal experience of Professor Oosthuizen.

Table 2. Stepwise treatment plan for an anxiety disorder – alternative drug if the initial drug used is ineffective or poorly tolerated[4,5]

Second-line drug treatment (less well tolerated or weak evidence base, no order of preference)	
Agomelatine 10-50mg/day	Agomelatine has been shown to prevent relapse over a 6-month period
Beta-blockers Propranolol 40-120mg/day in divided doses	Initiate at 40mg and titrate dose up to effect if needed. Useful for somatic symptoms, particularly tachycardia
Buspirone 15-60mg/day in divided doses	Has a delayed onset of action, takes up to 6 weeks to show equal efficacy with benzodiazepines
Hydroxyzine 50-100mg/day in divided doses	It is unclear whether hydroxyzine's efficacy is due to an anxiolytic effect or a sedative effect
Quetiapine (MR, 50-300mg)	Recommended as monotherapy. Probably not effective as adjunctive thearpy to SSRI/SNRI in treatment resistance

Adapted from Bandelow *et al,* 2008.[5]

Table 3. Maudsley guidelines 2018[6]

Drug	**Comment**
Crisis management	
Benzodiazepines	Normally for short-term use only: max. 2-4 weeks, although some are of the opinion that risks are overstated
First-line drug treatment (in order of preference)	
SSRIs (up to maximum licensed dose)	May initially exacerbate symptoms. A lower starting dose is recommended. Fluoxetine and sertraline are preferred options
SNRIs (up to maximum licensed dose)	May initially exacerbate symptoms. A lower starting dose is recommended.
Pregabalin 150-600mg/day in divided doses	Response may be seen in the first week of treatment

Cognitive behavioural therapy should be part of the treatment strategy in anxiety management

Table 4. Preferential therapies for individual anxiety disorders

Disorders	**Treatment**
Phobias	Psychotherapy (CBT and desensitisation) and SSRIs
Social phobias	CBT SSRIs, in particular paroxetine (beware of side effects)
Obsessive compulsive disorder	All medications can be helpful
Panic disorder	Citalopram is very useful *Not* fluoxetine

Therapeutic options include switching to an SNRI or to other agents with anxiolytic effects such as pregabalin, starting low with 25mg at night

Post-traumatic stress disorder	CBT Eye movement desensitisation and reprocessing (EMDR) Antidepressants	Carbamazepine can be useful *Not* debriefing *Not* a benzodiazepine
Separation anxiety disorder	Psychotherapy only	
Comorbidity with anxiety	Major depression – focus on the clinical management of this disorder first, ideally not treated at primary care level Bipolar disorder should not be treated at primary care level, and *not* with antidepressants	

Other treatments

Exercise has an important positive role to play in anxiety and, generally, in all mental health issues. Mindfulness and meditation are helpful.

Additional tips when prescribing antidepressants and other therapies for anxiety

- Beware of drug interactions
- Warn the patient about side effects
- Counsel the patient about missing a dose and why this is important
- Beware that the implications of missing a dose vary dramatically from patient to patient
- SSRIs should be first-line therapy as they have fewer side effects than SNRIs, although both classes are effective
- Of the available SNRIs in South Africa, duloxetine, venlafaxine and desvenlafaxine are vastly different molecules; duloxetine should not be used in patients with liver disease
- Tricyclic antidepressants are useful in the patient who cannot tolerate SSRIs or SNRIs, but there is a larger burden of side effects
- Pregabalin has good evidence for treating anxiety disorders. Although it is registered in the USA and Europe for this indication, this is not the case in South Africa. Pregabalin may make the patient sleepy
- Dopaminergic drugs (antipsychotics) are not ideal for use in primary care, and have a burden of side effects
- Benzodiazepines must be used appropriately and safely, i.e. intermittently for short periods of time. Discuss with a colleague if using for longer than three months
- Discuss side effects of any therapy with patients, working out a therapy plan to match the patient's circumstances. Stay up to date on new medications.

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