Therapeutic Management of Anxiety Disorders

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Anxiety disorders are among the most prevalent of mental disorders, afflicting about 13.3% of the general population (females 16%, males 9%) (Table 1). Although chronic and debilitating, these disorders remain under-diagnosed and therefore untreated, which leads to overuse of both psychiatric and non-psychiatric services. Anxiety disorders are also associated with an increased risk of suicide 10 times higher than that of the general population. Up to 75% of patients will have another comorbid psychiatric condition which can significantly increase suicidal behaviour.

Symptoms and onset

All anxiety disorder symptoms share the key features of psychological (worry, fear, apprehension) and physiological arousal (tachycardia, shortness of breath, stomach upset, sleeplessness) which lead to impaired functioning and distress. Onset of symptoms can be in childhood but is usually in adolescence or early adulthood depending on the type of disorder. It is rare to acquire these disorders beyond the age of 45, alerting the physician to secondary causes and the need for more extensive workups. When evaluating any patient, it is important to identify other potential causes. Several medical and psychiatric conditions and medications can exhibit secondary symptoms of anxiety (Table 2).

Alexander's case

Alexander, 45, is experiencing:

- Excessive worry
- Restlessness
- Easily fatigued
- Sleep disturbance

He also has a history of substance abuse but no current comorbidities. He was diagnosed with generalized anxiety disorder and started on buspirone.

Questions

1. Why was buspirone selected instead of either a benzodiazepine or an antidepressant?
2. Are there any psychotherapeutic therapies that could have been suggested for Alexander?

For more on Alexander, look to page 70.

Overview of treatment

All patients should receive psychoeducation about their anxiety disorder. Content should include information about their illness, general prognosis, treatment choices as well as self-help programs/strategies. Treatment choices for either psychological and/or pharmacological therapy, which can be used in combination or independently, depends on:

- patient preference,

Table 1

Common anxiety disorders

Panic disorder

Panic disorder is a series of spontaneous panic attacks which involve intense apprehension, fearfulness, or terror, often associated with feelings of impending doom. Accompanied by physical symptoms (*i.e.*, palpitations, chest pain, sweating, shortness of breath, nausea)

Generalized anxiety disorder (GAD)

GAD is unrealistic excessive anxiety and worry about events or activities persistent for most days for at least 6 months. Often accompanied by physical symptoms (*i.e.*, headache, muscle tension, upset stomach)

Phobic disorders

Specific phobia is characterized by significant anxiety provoked by exposure to a specific feared object or situation. Social phobia (social anxiety disorder) is a significant anxiety provoked by exposure to certain types of social or performance situations

Obsessive compulsive disorder (OCD)

OCD is characterized by obsessions (persistent thoughts, impulses or images) which cause marked anxiety and/or compulsions (repetitive behaviours or mental acts) which serve to neutralize the anxiety

Post-traumatic stress disorder (PTSD)

After experiencing an extremely traumatic event, PTSD is characterized by persistent re-experiencing of the event, avoidance of stimuli associated with the trauma, numbing of general responsiveness and accompanied by symptoms of increased arousal

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- motivation,
- availability of resources and
- concurrent psychiatric and/or medical conditions.

Psychological therapies, which have an important role in all anxiety disorders, include:

- cognitive-behavioural therapy,
- interpersonal therapy,
- supportive, brief psychodynamically-oriented therapy and
- hypnotherapy.

All classes of antidepressants have demonstrated a degree of efficacy in anxiety disorders with the exception of bupropion. Based on safety and efficacy evidence, antidepressants, especially the selective serotonin reuptake inhibitors (SSRIs) and venlafaxine, are considered first-line therapy for all the anxiety disorders. Advantages of therapy include safety in pregnancy, no dependency risk and treatment of other comorbidities including substance abuse. Limitations are delayed response, some stimulatory and sexual dysfunction with SSRIs and overdose potential with older antidepressants.

Benzodiazepines are effective, but risk of dependency and cognitive impairment, which can interfere with psychotherapy, limit them to second-line therapy. However, these agents can be used as adjunctive therapy briefly early in treatment if patients are experiencing extreme anxiety and agitation, until the other therapies begin to work.

Buspirone is a treatment option limited to generalized anxiety disorder. It has the advantage of no dependency, less cognitive impairment and no drug interactions, but has a delayed onset of up to two weeks.

Other options mostly considered second-/third-line are the newer anticonvulsant agents (gabapentin, lamotrigine, pregabalin, topiramate), the atypical antipsychotics (olanzapine, risperidone, quetiapine) and hydroxyzine, an antihistamine with sedative properties.

Medications which should be avoided during pregnancy because of their teratogenic potential include: paroxetine, benzodiazpines, MAOIs, lithium, valproic acid and carbamazepine.

Despite appropriate therapy, 40% of patients will experience residual symptoms or treatment resistance. The major causes for inadequate response include the presence of comorbidities, personality disorders, or environmental stressors. Treatment strategies include the use of second- or third-line agents as well as combination therapy.

Monitoring and follow-up

Antidepressants (and other agents) should be started at the lowest dose to assess tolerability and optimize adherence. The dose can be increased every one to two weeks until therapeutic doses are reached (Table 3). Improvement may take four to eight weeks or more. Patients should be monitored every two weeks (weekly for special populations, such as children, the elderly, or the medically ill) for the first six weeks, then monthly thereafter as required. The Clinical Global Impression (CGI) scale can be used to assess improvement as it is brief, comprehensive and simple to use. Patients who fail two first-line agents, should be referred to a specialist.

Table 2

Common medical illnesses and medications associated with anxiety

CV
- Angina, arrhythmia, heart failure, MI

Endocrine and metabolic
- Hyper/hypothyroidism, pheochromocytoma, electrolyte imbalance, diabetes, menopause

Pulmonary
- Asthma, chronic obstructive pulmonary disease, pneumonia

Others
- Pain, anemias, cancer, withdrawal from prescription drugs, caffeine

Medications
- Stimulants, bronchodilators, thyroid supplements, selective serotonin reuptake inhibitors (SSRIs), illicit drugs

Table 3

Dosages for commonly prescribed medications for anxiety

	Initial daily dose (mg)	Maximum daily dose (mg)
SSRIs		
citalopram	20	40-60
escitalopram	5-10	20
fluoxetine	10	80
fluvoxamine	50	300
paroxetine	20	60
sertraline	25	200
Benzodiazepines		
alprazolam	0.25	1.5-3.0
clonazepam	0.25	4
diazepam	2.5	10
lorazepam	0.5	3-4
Other agents		
buspirone	5	30
clomipramine	25	200
venlafaxine XR	37.5-75	225

Alexander's follow-up

Alexander described his symptoms as only slightly improved. His buspirone dose was increased to 30 mg q.d. Two weeks later he felt his symptoms were not controlled to his satisfaction and asked to be on benzodiazepine. He remembers it was more effective in taking off the edge of his anxiousness.

The buspirone was discontinued and venlafaxine XR was started at 75 mg q.d. and adjusted for efficacy and tolerability. Six weeks later, Alexander reports most of his symptoms are under control and he continues to show improvement.

Take-home message

- Psychological and pharmacological interventions are effective in treating all the anxiety disorders. Both therapies can be used to complement each other
- While some benefits may be seen as early as 1 week with antidepressant therapy, significant improvement may not be seen until 6 to 12 weeks
- In order to minimize relapse, pharmacotherapy should be continued for 1 to 2 years with regular monitoring
- Not all SSRIs have approved indications or demonstrate the same efficacy for the treatment of all the anxiety disorders
- Both the benzodiazepines and the antidepressants should be tapered over several weeks to minimize withdrawal symptoms

Anxiety disorder: specific tips

In panic disorder, antidepressants should be started at very low doses to prevent stimulatory side-effects such as insomnia or nervousness, which can affect adherence. Antidepressants are particularly effective in generalized anxiety disorders since many of the patients will have a comorbid psychiatric disorder." Buspirone is an anxiolytic option specific for generalized anxiety disorder which is best prescribed in a benzodiazepine-naïve patient. Many patients have done well on benzodiazepine monotherapy as long as they are carefully monitored. Specific phobias are only managed by psychotherapeutic interventions while social phobia (or social anxiety disorder) responds well to paroxetine, sertraline and venlafaxine. Although reports are inconclusive, ß-blocker therapy (propranolol 10 mg to 80 mg or atenolol 25 mg to 100 mg) may be particularly useful in performance anxiety. Obsessive compulsive disorder responds best to serotonergic antidepressants such as the SSRIs. Clomipramine is an alternative in severe or treatment resistant cases. Although combination therapy and higher doses may be necessary, the need for higher dosages is overstated and can lead to increased drop out rates. In posttraumatic stress disorder, SSRIs are the most effective agents to manage the symptom cluster of avoidance/numbing while having a variable effect on arousal and re-experiencing. Dx

Resources
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