Pharmacology and Prescribing in Anxiety

Abstract

In this article in the series of 'bite sized' pharmacology, we will look at the pharmacological actions of drugs used in the management of anxiety disorders. This article will outline the categories of anxiety disorder and pharmacological interventions required in these disorders with reference to current guidelines and formulary. It will illustrate the common therapeutic interventions in patients with general anxiety disorder, panic disorder, social phobia, post-traumatic stress disorder and obsessive compulsive disorder.

It will then go on to examine the main types of drug used and their pharmacodynamic actions. The management will be considered within the NICE guidance and evidence base. Exercises will be provided to help you apply this knowledge to your prescribing practice.

Anxiety

Anxiety is a normal, healthy emotion when experienced in situations where there is uncertainty or fear. In some people however, anxiety can become an intolerable part of their lives and becomes debilitating. In these cases, it can be considered a pathological form of anxiety disorder, requiring treatment to enable the person to resume and maintain a normal life. Anxiety can present with a wide and particularly complicated spectrum of symptoms, both physical (somatic) and psychological. A person with anxiety disorder may suffer physical or psychological symptoms or a mixture of both and experience them to varying degrees. They can be chronic in nature or acute and can be in response to a stressor. Diagnosis can be difficult with the possibility of a range of investigations in to exclude a physical cause for the symptoms.

There are diverse types of anxiety disorder which are classified according to symptoms and signs.

Classifications of Anxiety Disorder

Throughout this article the anxiety disorders will be considered under the following five headings, since these are the conditions that are most amenable to treatment with medication:

- Generalised anxiety disorder (GAD)
- Phobic disorders, including social phobia
- Panic disorder (PD)
- Obsessive compulsive disorder (OCD)
- Post-traumatic stress disorder (PTSD)

The National Institute for Health & Care Excellence (NICE) have produced guidelines for the diagnosis and management of anxiety disorders. These include QS53- Anxiety Disorders, CG113- Generalised anxiety disorder and panic disorder in adults: management, CG31- Obsessive-compulsive disorder and body dysmorphic disorder: treatment, CG26- Post-traumatic stress disorder: management and CG159- Social anxiety disorder: recognition, assessment and treatment.

Exercise

With reference to your own area of practice, explore the categories of anxious patients you deal with and establish the diagnosis of the condition within recognised guidelines and parameters.

Symptoms of Anxiety

Anxiety disorders can be found in section F40, F41, F42 and F43 of the ICD10 Classification (International Statistical Classification of Diseases and Related Health Problems 10th

Revision (ICD-10)-2016-WHO Version for 2016). In section F40 the anxiety disorders are categorised according to their typical causes and covers agoraphobia, social phobias and specific phobias. Section F41 covers general anxiety disorders. These are panic disorders, generalised anxiety disorder and mixed anxiety and depression. In Section F42 we find Obsessive Compulsive disorder, and in F43 is Post-Traumatic Stress disorder. Although these conditions differ in the specifics of their symptom manifestation there is a core set of symptoms which can be physical, psychological or emotional. These include, but are not restricted to:

1) Palpitations.
2) Sweating
3) Trembling or shaking
4) Dry mouth
5) Difficulty breathing, or perceived difficulty with or without chest discomfort
6) Nausea or abdominal distress
7) Feeling dizzy, unsteady, faint or light headed, fear of losing control or fainting
8) Fear of dying
9) Hot flushes or cold chills
10) Numbness or tingling sensations

Robertson (2016)

The primary goal of drug therapy, in conjunction with psychological therapies is to manage the symptoms of the anxiety state. Anxiety can be managed by pharmacological and non-pharmacological interventions, or in many cases a combination of the two. The patient or client should be involved in the decision-making process about treatment where appropriate. This can lead to a good therapeutic relationship and will improve adherence to any medication initiated. Many anxiety sufferers benefit from support groups or self-help material

and this should be offered where it is prudent to do so. Psychological therapies can be very helpful in the management of anxiety disorders and should be considered for all sufferers.

Pharmacological Interventions

There are a range of medications that can be used for the treatment of anxiety disorders. A summary of the commonest used can be seen in Table 1.

Table 1: Drugs Commonly Used in the Management of Anxiety

Anxiety Disorder	Drug Used	Class Examples
Panic Disorder	SSRI TCA	Citalopram Imipramine
Social Phobia	RIMA SNRI	Moclobemide Venlafaxine
OCD	SSRI TCA	Fluvoxamine Clomipramine
GAD	Benzodiazepine Other Antidepressant Azaspirodecanedione	Diazepam Trazodone Buspirone
PTSD	SSRI SSRI	Sertraline Paroxetine

Information from BNF online

Exercise

Using pharmacologically available resources such as textbooks, the BNF or online electronic medicines compendium, explore the range of anxiolytic medication available.

Reconcile this with your local policy on prescribing in anxiety and NICE Guidance.

Pharmacology of Individual Classes of Drugs

Many of the drugs commonly used to manage depression are also anxiolytic in nature (Neal 2016). As you can see form Table 1 the Selective Serotonin Reuptake Inhibitors (SSRI's) feature heavily.

Selective Serotonin Reuptake Inhibitors (SSRI's)

These drugs act selectively at serotonin neurones to produce their effects. In normal physiology serotonin is released from stores in the presynaptic neurones into the synaptic cleft where it goes on to activate serotonin sensitive receptors located on the post-synaptic neurone. After release and receptor activation the serotonin molecule is recycled back into the presynaptic neurone to be stored for future chemical release. This recycling is facilitated by a transporter located in the presynaptic neuronal membrane. When used as a treatment for anxiety the SSRIs inhibit the reuptake of serotonin from the synaptic cleft. This results in an increase in the amount of serotonin in the synaptic cleft available to stimulate receptors. This potentiation is known to have an anxiolytic effect (Robertson 2016). The SSRIs have, like many medications evolved over time with discoveries of newer drugs with slightly better side effect profiles. Early SSRI's like fluoxetine and paroxetine are still used, but more commonly prescriptions of these drugs will be for citalopram or sertraline. Not all SSRIs are suitable for all anxiety disorders and care should be used in selecting the correct drug at the correct dose once a diagnosis of the type of anxiety disorder has been made. Doses used in anxiety tend to be lower, especially at initiation, than used in depression and should be titrated up in accordance with patient response.

Benzodiazepines

Benzodiazepines, despite their tendency to provoke addiction with long term use, are still effective anxiolytics. If a decision to prescribe benzodiazepines is made it should only be for short term use and the patient should be monitored.

These drugs exert their effect by potentiating the normal action of gamma-aminobutyric acid (GABA), the main inhibitory neurotransmitter in the central nervous system. This acts to increase its inhibitory effect in the brain and results in decreased neuronal firing activity. This action can be anxiolytic at low doses and at higher doses can produce drowsiness, impaired alertness and sedation (Neal 2016). They can be used in treatment of acute anxiety states or as short-term adjunct to psychological therapy.

Tricyclic Antidepressants (TCAs)

The tricyclic antidepressants such as amitriptyline have been used extensively in the past to help manage anxiety. With the advent of better and safer drugs are not used in first line management of anxiety. They may be considered if a patient is not responding to other therapies. Clomipramine and imipramine can be used in phobic and obsessional states, but low dose initiation, slow titration and close monitoring are required. TCA's inhibit the reuptake of two major monoamines, noradrenaline (NA) and serotonin, in synapses in the brain. This means that there is more of the monoamine available in the synapse to act at the receptors and this has an anxiolytic effect. The drugs are not selective like the SSRI's and can act at other receptors leading to side effects such as sedation and anticholinergic problems such as urinary retention and constipation (Robertson 2016).

They are very dangerous in overdose situations as they can produce cardiac rhythm problems which can be fatal.

Betablockers

These are used to manage some of the autonomic symptoms that occur in anxiety. The drug propranolol is the most commonly used example and is helpful in anxiety states where symptoms such as sweating, palpitations and trembling are excessive or problematic (Neal 2016). It can be useful in states of social or performance anxiety, whereby being in a situation such as a social event, an interview or a presentation triggers the anxiety state. It has actions at beta 1 and beta 2 receptors where it is a competitive antagonist, blocking the effect of the normal agonist noradrenaline. The dose is lower than that which would be given of this drug when it is used for its primary purpose of treating high blood pressure and a typical dose is 40mg once daily increased to 3 times daily if needed to manage the symptoms (BNF 2018).

Other Drugs

Buspirone is an azaspirodecanedione drug which has non-sedating activity at serotonin receptors and is licensed for short term use in anxiety disorders. It can be given up to 45mg per day in divided doses. It has some effect on psychological symptoms such as poor concentration and irrational worry (Robertson 2016, BNF 2018).

Venlafaxine is a noradrenaline and serotonin specific re-uptake inhibitor which may have a quicker onset of action compared to SSRIs alone.

Trazodone is an antidepressant drug that increases the level of serotonin in the synaptic cleft in the brain. It is also thought to have some effect on noradrenaline potentiation. Its exact mechanism of action is unknown, but it is a powerful antidepressant with clear anxiolytic properties (EMC 2018). Doses used in anxiety are typically half of those used in depressive disorders, with a maximum daily dose of 300mg daily (BNF 2018).

*Moclobem*ide is a reversible inhibitor of monoamine oxidase type A (RIMA). Monoamine oxidase, an enzyme, is responsible for the breakdown of the monoamines (mainly serotonin

and noradrenaline) in the synaptic cleft, thereby inactivating their action at receptors. By inhibiting the enzyme, we potentiate the time spent by the monoamines in the synapse and therefore their action at receptors.

Exercise

Using pharmacologically available resources such as textbooks, the BNF or online electronic medicines compendium, look up the specific class and modes of action of drugs you regularly expect to prescribe. Use this information to augment your personal formulary knowledge.

Stock Photo

NICE Guidelines give a good overview of which anxiolytic is most appropriate depending on the diagnosis and the individual characteristics of the patient, but it is important that we consider how to apply the guidelines within the context of the actual patient in front of us and ensure that we do not blindly and rigorously apply the guidelines, but rather use them to tailor a patient specific plan for the people we are prescribing for.

Exercise

Access the NICE guidance and choose, for a typical patient from your area of practice, the most appropriate first line treatment based on evidence.

References & Further Reading

BNF Online via NICE2018 https://bnf.nice.org.uk/

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