Chapter

Anxiety Disorders

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Abstract

Anxiety disorders are the most common of all psychiatric illnesses and result in significant functional impairment and distress. In DSM 5, anxiety disorders are divided into eleven subgroups. Anxiety, which we consider normal (mild and moderate anxiety), plays an important role in the development of the individual. However, if the level of anxiety increases, it may lead to mental problems. A high level of anxiety, long duration, and intensification of anxiety symptoms may cause anxiety disorders. These are; separation anxiety disorder, selective mutism, panic disorder, agoraphobia, specific phobia, social anxiety disorder, generalized anxiety disorder, other unspecified anxiety disorder, anxiety disorder related to another medical condition, anxiety disorder caused by substance or medication, anxiety disorders caused by substances and medication are unspecified anxiety disorders. Treatment methods used in anxiety disorders are individual psychotherapy, cognitive therapy, behavioral therapy, systematic sensitization, exposure, and psychopharmacology.

Keywords: anxiety disorders, panic disorder, phobia, social anxiety disorder, generalized anxiety disorder, selective mutism

1. Introduction to anxiety disorders

1.1 Anxiety concept

Anxiety is a feeling that individuals experience at different levels throughout their lives. Anxiety is a healthy, normal response to perceived threats or unique experiences, and it is a necessary motivating force for survival. Mild anxiety is a driving force necessary for adaptation and advancement to the higher stage of spiritual development. However, when the anxiety level increases too much, it, on the contrary, serves as a hindering function [1].

1.2 Anxiety and fear

Anxiety and fear are emotions that people are usually confused about. Fear is a response to a known threat. However, anxiety can be defined as fear, tension, uneasiness, or restlessness expected from an unidentified or unknown source. We can evaluate anxiety as a cognitive state of fear [2]. Physical symptoms of anxiety include palpitations, difficulty breathing, rapid breathing, tremors in the hands and feet, and excessive sweating. Psychological symptoms, on the other hand, include distress, excitement, sudden feeling, and fear that something terrible will happen [3].

Anxiety, which we consider normal (mild and moderate anxiety), plays an important role in the development of the individual. However, if the level of anxiety increases, it may lead to mental problems. A high level of anxiety, long duration,

and intensification of anxiety symptoms may cause anxiety disorders. Anxiety can be evaluated as pathological when it begins to have an impact on social and occupational actions, achievement of desired goals, and emotional state [4].

In short, anxiety can be deemed pathological if the following situations occur:

a. When anxiety is not proportional to the situation that creates anxiety,

b. When anxiety inhibits social, occupational, and other important functional areas.

Example: Ms. M., who was involved in a serious traffic accident a month ago, refuses to drive even to places in short distances. Her father has to take Ms. M. whenever she needs to go somewhere. Ms. M., who constantly refuses to drive, has even had to quit her job because of her anxiety about driving.

1.3 Epidemiology

Anxiety disorders are the most common of all psychiatric illnesses and result in significant functional impairment and distress [5, 6]. Its prevalence per year is reported as 17.7%. This rate is 30.5% for women and 19.2% for men, and the frequency decreases with the increase in socioeconomic level [7]. In a study conducted by Özcan et al. (2006), anxiety disorder was found to be the most common diagnosis among 950 psychiatric patients, and it was mostly observed in women, housewives, married people, and people with a low education level [8].

2. Etiology of anxiety disorders

2.1 Biological factors

In twin studies conducted, it was concluded that genetics was a huge factor. Structural neuroimaging studies in patients with panic disorder indicate pathological involvement in the temporal lobes, especially in hippocampus [9].

Although many neurotransmitters are effective in the pathophysiology of anxiety disorders, disorders in serotonin, norepinephrine, and gamma-aminobutyric acid (GABA) appear to be the most important. GABA has an important place among the causes of anxiety disorder. As the drugs used in the treatment of anxiety disorders increase GABA, it is thought that the insufficiency and imbalance in GABA are directly related to the anxiety experienced [3, 5]. Serotonin is another neurotransmitter linked to anxiety disorder. Deficiency or an imbalance of serotonin in the amygdala is observed in anxiety-related disorders. It is known that there is imbalance in the regions related to norepinephrine in anxiety disorders.

It has been revealed that the CRF (Corticotropin-Releasing Factor) system plays an important role among the biological causes of anxiety disorders [1].

2.2 Brain areas affected in anxiety disorders

The brain areas affected by anxiety disorders and the symptoms they cause are listed below:

- Amygdala: Fear, which is especially important in panic and phobic disorders.

- Hippocampus: Depends on memory which is related to fear responses.

- Locus coeruleus: Vigilance
- Brain stem: respiratory movement, heartbeat
- Hypothalamus: activation of the stress response
- Frontal cortex: Cognitive interpretations
- Thalamus: Integration of sensory impulses
- Basal ganglia: Tremors [10]

3. Psychological theories

Psychodynamic Theory: According to the psychodynamic view, anxiety is a state of tension that emerges in the self as a result of threats originating from within and outside the individual. Starting from childhood, repressed emotions, desires, impulses, experiences occasionally disturb the individual's self in the following years. A conflict arises between the self (ego), lower self (id), and upper self (superego), which creates anxiety in the individual. Anxiety is a harbinger of danger to the self, and the self tries to reduce anxiety by using self-defense mechanisms [11].

Freud argued that the child experiences anxiety specific to each period during the development process. These are superego anxiety, castration anxiety, fear of losing love, separation anxiety, annihilation anxiety, and disintegration anxiety.

Behavioral Theory: According to this theory, anxiety is an emotional experience developed based on the urge to escape from congenital pain or suffering. This theory suggests that if an individual experiences intense fears and stressful events in early periods of life, s/he is likely to experience high levels of anxiety in his/her later life. Fear responses acquired through conditioning, observation, and social learning cause "escape" and "avoidance" behaviors to be triggered, thereby reducing anxiety. The escape and avoidance behaviors are thus reinforced, and when any kind of anxiety is experienced, they come into play and the anxiety is prevented from fading. Thus, the continuity of anxiety is ensured in this way [11].

Cognitive Theory: In Beck's theory, how we interpret and perceive events determines our emotions; in other words, it is the meaning attributed to them rather than the events themselves that trigger our emotions. This interpretation depends on the characteristics of the environment in which the event occurs, the mood at the time of the event, and the past experiences of the individual. Individuals experience anxiety due to their false reasoning and irrational beliefs [1, 3].

4. Classification of anxiety disorders

In DSM 5, anxiety disorders are divided into eleven subgroups. These are:

- Separation anxiety disorder,
- Selective mutism,
- Panic disorder,

- Agoraphobia,
- Specific Phobia,
- Social anxiety disorder,
- Generalized anxiety disorder,
- Other unspecified anxiety disorder,
- Anxiety disorder related to another medical condition,
- Anxiety disorder caused by substance or medication,
- Anxiety disorders caused by substances and medication are unspecified anxiety disorders [12].

4.1 Separation anxiety disorder

Separation anxiety disorder can be defined as experiencing fear and anxiety that is more than expected and repetitive in terms of developmental level resulting from separation from home or someone the person is attached to for at least four weeks in children, and for at least six months or longer in adults. It is seen that individuals with separation anxiety disorder do not want to go to school or elsewhere because of the fear of separation. The main feature of separation anxiety disorder is excessive anxiety caused by leaving the mother, father, home or familiar environment. It is seen equally in boys and girls.

Etiology: According to the psychodynamic approach, children who are attached ambivalently are very busy with the care of their caregivers, which reduces their exploration behaviors of their environment and thus causes separation anxiety to develop. Stressful events such as parental divorce, illness, loss are important risk factors for separation anxiety disorder. In a study, it was found that the depressive, cyclothymic, irritable and anxious temperament scores of the mothers of children with separation anxiety disorder were higher than the control group [13].

Symptoms in separation anxiety disorder differ according to the developmental period. In children aged 5-8 years, the fear of a bad event and rejection of school, intense distress during separation at the age of 9-12, school refusal in adolescents aged 13-16, and physical complaints appear as symptoms.

Comorbidity: Frequently, depression, bipolar disorder, hyperactivity disorder, personality disorders and other anxiety disorders are seen together.

Treatment: In the treatment of separation anxiety disorder, the most important point is planning to include the family, school and child. Cognitive therapy is one of the effective methods. Antidepressants, selective serotonin reuptake inhibitors, are used in drug therapy. One study suggested that vilazodone can be used in the treatment of separation anxiety disorder [14].

4.2 Selective Mutism

The most important feature of this disorder is that although the individual can speak in other situations, s/he constantly does not speak in certain specific social situations (when s/he meets people s/he does not know, etc.) where s/he is expected to speak. The disorder must last at least one month and affect the person's education, work success, and social life. It usually occurs in the preschool period.

Etiology: In the etiology of the disorder, there are reasons such as delay in language development, communication defects, lack of communication, presence of psychiatric disorders in the family, and overprotection of the family.

Comorbidity: Social phobia, obsessive-compulsive disorder, speech and language disorders are among the disorders accompanying selective speech disorders.

Treatment: Behavioral treatments, pharmacological treatments, group and family therapies are effective in treatment. It has been stated that the cognitive-behavioral approach especially encourages verbal and non-verbal forms of communication. In family therapy, it is important to identify healthy and dysfunctional family relationships and to raise awareness of family members about unhealthy communication patterns and behaviors. Selective serotonin reuptake inhibitors are preferred in pharmacological treatment.

4.3 Panic disorder

In the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [American Psychiatric Association (APA)] it is stated that at least four of the following symptoms must be present to determine the presence of a panic attack. These are:

- Palpitations, pounding heart or accelerated heart rate
- Sweating
- Shaking or trembling
- Feeling short of breath or smothering
- Choking sensation
- Chest pain or discomfort
- Nausea or abdominal distress
- Feeling dizzy, lightheaded, unsteady or faint
- Chills or hot flushes
- Paresthesias (tingling and numbness sensations)
- Derealization (unreal feelings) or depersonalization (feelings of being detached from oneself)
- Fear of losing control and going crazy
- Fear of dying [12]

Panic disorder, which is a very old disease, is a syndrome characterized by sudden and extreme anxiety with unreasonable and unpredictable panic attacks. Its most important feature is that it is accompanied by intense physical discomfort. Panic attacks can occur only once, or frequently, on a weekly, monthly or even annual basis. Panic attack disorder is usually seen in the 20s. The panic attack is an unreasonable and severe state of anxiety. During panic attacks, symptoms such

as palpitations, accelerated heart rate, sweating, trembling/shaking, shortness of breath, feeling of choking, breathlessness, chest pain, fainting, fear of losing control or going crazy, numbness, tingling, chills or hot flushes can be seen.

The presence of a medical drum that may cause anxiety should first be investigated in a patient presenting with panic attack. All the drugs used by the individual should be questioned, and the side effects of the drugs should be considered. Below are some medical conditions that cause symptoms similar to panic attacks.

Certain medical conditions that produce symptoms similar to panic attacks

- Alcohol Withdrawal Syndrome
- Substance Withdrawal Syndrome
- Cardiac arrhythmias
- Hyperthyroidism
- Hypoglycemia
- Asthma
- Cushing's Disease

The majority of patients have challenging life events before the first panic attack occurs. Low socio-economic level, delay in treatment, presence of additional diagnoses cause a negative course in panic disorder.

Comorbidity: Depression is seen with social phobia, specific phobia, traumatic stress disorder and alcoholism.

Treatment: Specific serotonin reuptake inhibitors should be the first choice in the treatment of panic disorder. If the patient does not respond to treatment, switching to other specific serotonin reuptake inhibitors is recommended. If there is no response to two specific serotonin reuptake inhibitors and there is severe tolerance, it is recommended to switch to SNRI. Alprazolan is also highly effective. Drug treatment should last at least a year. Behavioral-cognitive psychotherapy is an effective method in panic disorder. This method attempts to change the patient's perception of physical symptoms. It will be useful to teach breathing exercises to the patient [15].

4.4 Agoraphobia

Agoraphobia, which is shortly defined as the fear of open space, is the fear of being deprived of help or being in places where it is difficult to escape.

Treatment: Combination of pharmacotherapy and psychotherapy (behavioral, cognitive, virtual therapies) is recommended in its treatment. Benzodiazepines, SSRIs, tricyclic and tetracyclicantidepressants are recommended as diocological [15].

4.5 Social phobia (social anxiety disorder)

It is a disorder characterized by blushing, sweating, and trembling of the hands when one believes that s/he is perceived negatively by others while sitting or talking in public. The individual is afraid of social or performance situations where embarrassment can occur and firmly believes that s/he will be subject to possible reproach by others [12]. The onset of the symptoms of this disorder often occurs in

late childhood or early adolescence and becomes chronic and sometimes continues throughout life. It is equally prevalent in males and females (Puri & Treasaden, 2011). The disorder affects social or occupational functionality or causes significant distress.

Treatment: In its treatment, the combination of psychotherapy and pharmacotherapy has an advantage over the individual application of both treatments. The drug groups to be used in the treatment of social phobia similar to other anxiety disorders are SSRIs, benzodiazepines, venlafaxine and busprone. MAO inhibitors such as phenelzine and moclobemide have been shown to be successful in severe cases [15].

4.6 Specific phobia

It is an excessive, illogical and meaningless fear of a specific object (snake, dog, etc.) or a situation (injection, darkness, etc.). Exposure to phobic stimulus produces compelling panic symptoms, including palpitations, sweating, dizziness and difficulty in breathing. Phobias can begin at any age. People can be phobic towards almost any object or situation. Those that start in childhood often disappear without treatment. But those that start in adulthood or are persistent often require therapeutic support. The disorder is diagnosed more often in females than in males [16]. The specific classification of simple phobias is given in **Table 1**.

Treatment: It is not enough to use drugs alone in the treatment of specific phobias. Behavioral therapy, insight-oriented therapy, virtual therapy and pharmacotherapy are at the forefront in its treatment [17]. The main principle of treatment should be exposure to the feared situation. When the phobia is accompanied by panic attacks, beta-adrenergic receptor antagonists or benzodiazepines can be used. The combined use of pharmacotherapy and psychotherapy may also be effective.

4.7 Generalized anxiety disorder

It is an anxiety disorder characterized by being chronic and unrealistic, and extreme anxiety that must last at least 6 months. Symptoms can cause distress to the person in social, professional and other important areas. Individuals with this disorder are constantly worried. Restlessness, excessive excitement, fatigue, sleep disturbance and muscle tension are significant symptoms. Anxiety often results in difficulty in making self-decisions, and the person seeks constant approval from those around him. They always feel like they are going to get bad news. It usually starts in childhood and adolescence [2].

Comorbidity: It is seen with depression and other anxiety disorders.

Treatment: Cognitive-behavioral, supportive and insight oriented therapy and pharmacotherapy have a role in its treatment. The main drug groups used in the

Clinical name	Feared object or situation
Acrophobia	Heights
Agoraphobia	Open spaces
Claustrophobia	Closed spaces
Hematophobia	Blood
Zoophobia	Animals

Table 1.
Specific classification of simple phobias.

treatment are benzodiazepines, SSRI, buspirone and venlafaxine. Benzodiazepines in treatment should be started with the lowest dose of the therapeutic range to be used and the dose should be increased in case of unresponsiveness [1].

4.8 Anxiety disorder associated with another medical condition and substance/ medication-induced anxiety

Symptoms associated with these disorders are evaluated directly as a physiological consequence of another medical condition or directly due to substance intoxication or deprivation or exposure to the drug. Many medical conditions are related to the development of anxiety symptoms. Some of these include cardiac conditions such as myocardial infarction, congestive heart failure and mitral valve prolapse, endocrine conditions such as hypoglycemia, hypo/hyperthyroidism and pheochromocytoma, respiratory conditions such as chronic obstructive pulmonary disease and hyperventilation, and complex partial seizures, neoplasms and encephalitis [12].

5. Treatment methods in anxiety disorders

5.1 Cognitive - behavioral therapy

It is a widely used, successful and easy method in the treatment of anxiety disorders. This short-term treatment method focuses on changing the patient's thoughts and behaviors. This treatment includes emotional and behavioral changes to help the person to adapt to the environment perceived to be dangerous, as well as the initial definition and restructuring of cognitions related to anxiety in the form of unreal interpretation of danger [9, 18–20]. In their study, Andrews et al. (2005) also found that virtual reality practice therapy is effective in treating public speaking anxiety [21].

5.1.1 Systematic desensitization

In systematic desensitization, the patient is gradually exposed to the effect of phobia stimuli in real or imaginary situations. The concept was first introduced by Joseph Wolpe in 1958 and is based on the principles of behavior conditioning. Emphasis is placed on mutual inhibition or mutual conditioning [22].

Mutual inhibition is defined as limiting anxiety before trying to reduce avoidance behaviors. The rationale behind this concept is that individuals cannot be excited and relaxed at the same time, as relaxation is the opposite of anxiety [23].

There are two important elements in systematic desensitization by mutual inhibition:

1. Practicing relaxation techniques

2. Gradual exposure to fear stimuli in a relaxed state.

The individual is taught the art of relaxation by using techniques that are more effective for him/her (e.g. progressive relaxation, mental imagination, tension and relaxation, meditation). After the individual learns relaxation techniques, exposure to phobic stimuli is initiated. The patient is asked to rank hierarchically the situations that cause phobic stimuli from the most disturbing to the least disturbing. In case of maximum relaxation, the patient may be asked to visualize the phobic stimulus in his/her mind. First of all, the exposure focuses on the phobic stimulus that

causes the least fear or anxiety. In subsequent sessions, the individual is exposed to the effects of increasingly more fearful stimuli. Sessions can be conducted in imaginary, real-life situations (live), or sometimes a combination of both [1].

5.1.2 Flooding therapy

Flooding is the therapeutic process that involves the patient participating in real-life events or imaginary situations that s/he thinks to be extremely fearful for a long time. Relaxation training is not part of the technique. Such sessions should be given a long period because short periods can be ineffective and even harmful. The sessions are terminated when the patient reacts significantly less than s/he did at the beginning of the sessions [24].

5.1.3 Relaxation exercise

Relaxation exercise is a method that effectively reduces tension and anxiety. It can be used alone or in conjunction with other cognitive-behavioral techniques [25].

5.2 Family therapy

Families have difficulties in understanding the symptoms of their relatives with anxiety disorders and may find it hard to tolerate, and this situation can disrupt the healthy family structure. It is important to remind family members of their roles in therapy and to emphasize that support is important. Besides, it is necessary to inform them about anxiety disorder symptoms and treatments [1]. In another study conducted, it was concluded that treatments aimed at reducing symptoms only were insufficient in the treatment of anxiety disorders and that programs for improving interpersonal relationships, communication skills and anger management of the individual should be added [26].

5.3 Psychopharmacology

Anxiolytics: Benzodiazepines are used successfully in the treatment of common anxiety disorders. It can be prescribed when the patient is particularly anxious. Alprazolam, lorazepam and clonazepam are particularly effective in treating panic disorder. In Benzodiazepine *treatment*, there are physical addiction and tolerance risks that can lead to addiction. This is because deprivation symptoms can be life-threatening, so patients should be warned against sudden termination of drug intake, and drug termination should be done with treatment. Due to potential for addiction, benzodiazepines, SSRIs, serotonin, and norepinephrine reuptake inhibitors (SNRs), and buspirone are the first-line therapy [27].

Buspirone, which as an anti-anxiety agent, is effective in approximately 60% to 80% of patients with a generalized anxiety disorder [3]. The only disadvantage of buspirone is the 10-14 day delay in relieving symptoms. However, the lack of physical addiction and tolerance disadvantage of buspirone makes it the drug of choice in the treatment of generalized anxiety disorders. The effects and side effects of anxiolytic agents are given in **Table 2**.

Antidepressants: Many antidepressants are as effective as anti-anxiety agents. Tricyclic, clomipramine and imipramine drugs are used successfully in patients with panic disorder. However, after the discovery of SSRIs, tricyclics are used less frequently because they tend to cause side effects when given in desired high doses to alleviate panic disorder symptoms [15].

Anxiolytic agents	Effect	Side effects
Benzodiazepines	The GABA receptor increases the affinity of GABAA.	Sedation, dizziness, weakness, ataxia, decreased motor performance, addiction, withdrawal
SSRIs	Inhibiting serotonin reuptake at the presynaptic nerve end, increasing serotonin synaptic concentration.	Nausea, diarrhea, headache, insomnia, sleepiness, sexual dysfunction
SNRIs	Inhibition of neural serotonin and norepinephrine reuptake, mild reuptake of dopamine	Headache, dry mouth, nausea, drowsiness, insomnia, weakness, dizziness, constipation, diarrhea
Noradrenergic agents (propranolol, clonidine)	Propranolol: inhibits beta adrenergic receptor activity. Clonidine: stimulates alpha-adrenergic receptors.	Propranolol: bradycardia, hypotension, weakness, fatigue, impotence, gastrointestinal disorder, bronchospasm
Barbiturates	CNS depression also produces effects in the hepatic and cardiovascular systems.	Clonidine: dry mouth, sedation, fatigue, hypotension
Buspirone	5-HT1A receptor partial antagonist	Drowsiness, agitation, confusion, ataxia, dizziness, bradycardia, hypotension, constipation

Table 2.
Anxiolytic agents.

SSRIs are effective in treating panic disorders. Paroxetine, fluoxetine, and sertraline have been approved by the US Food and Drug Administration (FDA) for these purposes. The dosage of these drugs should be increased gradually, as patients with panic disorder are sensitive to overstimulation caused by SSRIs [1].

The use of anti-depressants in the treatment of generalized anxiety disorders is still under investigation. Some success has been reported with tricyclic, imipramine and SSRI drugs. The FDA has approved paroxetine, escitalopram, duloxetine and extended-release venlafaxine for the treatment of generalized anxiety disorders [28].

Beta blockers: Clonid and beta-blockers such as propranolol and atenolol are also used especially in maintenance treatment. These drugs are most effective in treating state anxiety [1].

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