



Review Article

AN OVERVIEW ON ANXIETY : ETIOLOGY AND THERAPY

Angel Mary, Jyothi.Y*, Saifulla Khan and Anuja Ranjan

Krupanidhi College of Pharmacy, 12/1 Chikkabellandur, Carmelaram Post, Bangalore - 35, India

Abstract

Purpose: Anxiety disorders have turned out to be the most common mental health conditions prevailing all over the world. The symptoms of anxiety are very common in the community, not only affecting the younger generations but also the elderly. There have been a number of advances in the pharmacotherapy of anxiety disorders in recent decades. Normal anxiety is a kind of emotion that mainly helps to face the threats and problems awaiting an individual. But when this emotion exceeds a certain limit, it causes harm to the same individual. Thus, this paper gives an overall review on what exactly anxiety is, how it is caused and the different treatment methods used so far for anxiety. Apart from this the future aspects has also been covered in this paper.

Approaches: The data were collected from various sources like journal articles, textbooks, internet, related materials in library and databases such as pubmed, google scholar and so on.

Findings: New developments are forthcoming in the field of alternative strategies for managing anxiety and for treatment-resistant cases.

Conclusion: As a word, anxiety may seem very small to read but when it comes to a person's life it can be life threatening. There are varieties of conventional treatment methods available for anxiety and many promising therapies are yet to come.

Keywords: *anxiety disorders, epidemiology, Psychological treatments, Psychotherapy, Antidepressants.*

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INTRODUCTION

Apparently we all face physical, mental, emotional and social challenges in our day to day life¹. It is normal to feel anxious especially when facing a tough and challenging situation, attending a job interview or cracking a tough exam. But when these fears dominate and interrupt our daily activities, it leads to anxiety disorders. Anxiety is a state of emotion that is not pleasant in nature and is often associated with uneasiness, discomfort and concern or fear about some future threat². Nearly one-eighth

of the total population throughout the world is subjected to anxiety and thus it has become a very important area of research interest³.

Anxiety disorders usually last for many years and are characterised by depression, decreased quality of life and increased mortality⁴. There are many different ways for treating anxiety, the main treatment being psychopharmacological and cognitive behavioural therapy. Still researches are being conducted to use a combination of these treatment methods for the improvement of future complications.

Symptoms

Anxiety not only affects our body but it also affects ones thoughts and behaviour. It becomes a problem when the person's body reacts to an imaginary danger. An anxious person is subjected to a number of sensations in the body. These sensations are nothing but the body's natural reaction to the

*Corresponding Author:

Jyothi. Y

Associate Professor

Dept. of Pharmacology

Krupanidhi College of Pharmacy, Bangalore - 35

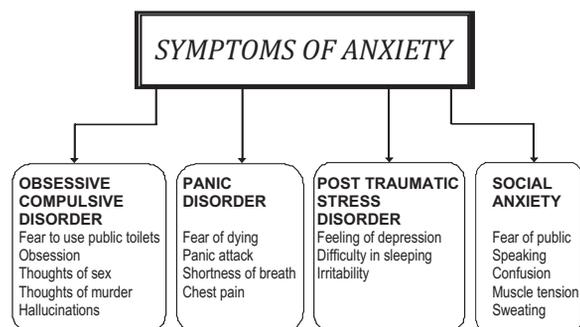
Phone : 07259519535

Email: jokiran05@gmail.com

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evading dangers. Experiencing anxiety mainly depends on two components namely physical and emotional components⁵. Physical sensations include nervousness, worry, fear, irritability, isolation from others, insecurity, desire to escape, feeling that one is going to die etc. While emotional sensations include headache, nausea, vomiting, sweating, trembling, stomach pain, diarrhoea, ulcers, weakness, body ache, shortness of breath.



Etiology

As such the exact cause of anxiety is not known, although a number of factors have shown involvement in its cause⁶. However anxiety, like other forms of mental illness is not caused due to personal weakness or flaw in ones character. But it occurs due to involvement of several factors like genetic, biochemical and social factors.

Genetic factors

Evidences suggest that genetic factors play an important role in causing anxiety⁷. A chance of anxiety disorder in a person whose family is already suffering from the disorder is higher⁸. Even though certain genes are involved in provoking anxiety, but it is not necessary that such disorder will only develop due to a single gene. In turn a number of genes have been associated with anxiety like PLXNA2, SERT, CRH and COMT⁹. Some of the genes even have an impact on neurotransmitters and hormones, which are somehow directly related to anxiety. Apart from this many other factors also play a key role in anxiety.

Brain chemistry

Several studies have shown that neurotransmitters present in brain are directly associated with the development of anxiety¹⁰. Abnormal levels of neurotransmitters can cause generalised anxiety disorder. Neurotransmitters are the brain's chemical

messengers that transmit signals between brain cells. The three main neurotransmitters responsible for causing anxiety are serotonin, norepinephrine and gamma amino butyric acid (GABA).

Apart from this certain changes in brain activity also leads to anxiety. These changes may include abnormalities in cerebral blood flow and metabolism, changes in the activities in locus ceruleus etc.

Social factors

Some of the life experiences like stress from job or job loss, financial issues, severe medical illness, death of a loved one, divorce may also contribute to anxiety disorders. Long term exposure to violence, poverty, illness and abuse has an increased impact on anxiety¹¹.

Other factors

Several other factors that cause anxiety include substance use and abuse, environmental and external factors like stress at work, lack of oxygen at high altitude, psychological factors like behavioral changes, spiritual concerns¹². Health problems such as asthma, heart diseases, cancer and diabetes can lead to anxiety¹³. Differences in personality can also significantly affect the development of anxiety disorder in an individual.

Epidemiology

It has been reported that approximately 500 million people all over the world suffer from mental distress¹⁴. Most of the disabilities and deaths occur as a result of mental impairments. This in turn increases the risk of physical illness as well as mortality. Mostly anxiety disorders appear during childhood and scientifically proven evidences show that most children continue to have such disorders even after they grow up¹⁵. Depression, a form of anxiety disorder is amongst the most common causes of mental problems.

It has been reported that women are more prone to anxiety disorders than men. As they are very common, anxiety disorders have a major impact on economy¹⁶. They affect productivity due to job loss as well as financial stress. Effect of anxiety disorder on an individual is so severe that it leads to depression, alcohol or substance abuse or personality disorder¹⁷.

Treatment and Therapy

Several treatment methods have been discovered in

the last few decades for the people suffering from anxiety. Even though a number of treatment options are available, still less than 30% of the individuals suffering from the disorder opt for treatment¹⁸. Before beginning the treatment, proper and careful diagnostic evaluation of the individual is carried out to determine if the symptoms are caused due to anxiety disorder or due to any other physical problem.

If the disorder has been diagnosed, the types of disorder or the combination of disorders that are present are identified depending on which type of therapy or treatment approaches are opted. The most common varieties of treatment for anxiety disorders are psychotherapy and medication. In order to increase the effectiveness of the treatment in certain cases, a combination of psychotherapy and drug therapy is considered appropriate than individual treatment approaches¹⁹.

Psychological treatments

Psychotherapy has been considered the first choice of treatment. However, in certain exceptional cases where anxiety becomes so severe that immediate treatment is needed to prevent any further complications, the following therapies come into picture.

- Behavioral therapy:-These emphasize on using techniques such as guided imagery, relaxation training, biofeedback (to control stress and muscle tension) and exposure with response prevention²⁰. These techniques are achieved by gradually exposing the person to the object or the situation that he fears the most. A therapist will often accompany the person to provide mental support and guidance.
- Cognitive behavioral therapy (CBT):-CBT has been proven to be the most effective form of treatment for anxiety disorders and has received enormous amount of empirical support. In this therapy, people learn to deal with fears by modifying their ways of thinking, behaving and reacting to anxiety producing and fearful situations. It has been scientifically proven that CBT is effective for several anxiety disorders, particularly panic disorder and social phobia²¹. In case of social anxiety disorder, CBT can help people learn and practise social skills.

The two specific components of CBT are cognitive therapy and exposure (behavioral) therapy. Cognitive therapy helps people change their thinking patterns by focussing on identifying, challenging and then neutralising unhelpful thoughts. Exposure therapy focuses on changing people's reactions to anxiety provoking situations. The person confronts the things he or she fears by engaging in activities he or she has been avoiding. This therapy is used along with relaxation exercises. CBT can be conducted on an individual person or a group of people who have similar problems.

- Psychotherapy:-Psychotherapy or “talk therapy” can help people with anxiety disorders. It mainly aims in resolving mental conflicts and stresses, as well as try to bring out and treat the several aspects of anxiety disorders solely through talk therapy. This is done by having a face to face conversation with a trained mental health professional such as psychologist, psychiatrist, social worker or a counsellor so that the person learns how to deal such disorders²².
- Family therapy and parent training:-The fact that a person may develop anxiety disorders due to family issues cannot be taken lightly. Thus, this therapy mainly focuses on the family and its dynamics. It may be assumed that the individual of a family may suffer from mental turmoil due to the rising conflicts that may occur among the family members. Thus each member is expected to contribute in resolving the conflict or the problem that is being addressed.

Pharmacological treatments (medication)

Research has shown that people suffering from anxiety disorders often get relief with medications such as benzodiazepines, azapirones, tricyclic anti depressants. These medications mainly affects various neurotransmitters particularly serotonin, norepinephrine and GABA. Such medications can only be prescribed by a medical doctor. These help in reducing symptoms of anxiety especially when combined with cognitive behavioural therapy. The most important classes of medications used to combat anxiety disorders are anti depressants, anti anxiety drugs and beta blockers.

Antidepressants

Antidepressants are considered to be the first choice of drugs for the treatment of anxiety disorders. These are prescribed because of their safety, efficacy and non addictiveness and do not show any long term effects. But the fact that these medications do have side effects cannot be left unnoticed. For some people, the side effects are mild while for others it may be more troubling. Several anti depressants are potent inhibitors of cytochrome p450 enzymes²³. These drugs are more beneficial in cases where anxiety and depression occurs together²⁴. The sub classes of antidepressants include selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, tricyclic and tetracyclic antidepressants and Monoamine oxidase inhibitors.

Selective serotonin reuptake inhibitors (SSRIs)

These drugs are also known as serotonin specific reuptake inhibitors²⁵. SSRIs are usually used in case of depression and include fluoxetine, sertraline, citalopram, escitalopram, fluvoxamine, paroxetine and vilazodone²⁶. These drugs act by inhibiting the serotonin transporter and cause desensitization of postsynaptic serotonin receptors, thus bringing back the activity of serotonergic pathways to normal.

Common side effects include sexual inhibition, gastrointestinal complaints, weight gain, headaches and sedation.

Serotonin norepinephrine reuptake inhibitors (SNRIs)

These include venlafaxine, desvenlafaxine and duloxetine²⁷. The main mechanism of action includes inhibition of serotonin and norepinephrine transporters. These are used when SSRIs fail to treat anxiety disorders or show inadequate response since SNRIs are considered to be as effective as SSRIs²⁸. Common side effects include nausea, drowsiness, dizziness, fatigue, loss of appetite and sexual dysfunction. In higher doses, venlafaxine may increase blood pressure.

Tricyclic and Tetracyclic antidepressants

All tricyclic antidepressants cause norepinephrine reuptake inhibition and most of them also mediate serotonin reuptake inhibition. These drugs are rarely used in the treatment of anxiety disorders as they produce adverse effects to a greater extent and are

lethal in case of overdose. However, clomipramine is one such drug that is considered safe and effective²⁹. These may interact with certain medications especially medications used to treat heart diseases. Common side effects include dry mouth, tremors, constipation, sedation, blurred vision.

Monoamine oxidase inhibitors

These are highly effective medications used for the treatment of depression and anxiety. Due to their dietary complications and side effects, they are used very rarely. They may interact with tyramine or dopa containing food substances thus causing severe high blood pressure, which may be life threatening. Tyramine is a protein found in foods that are fermented or high in yeast. Common adverse effects include nausea, postural hypotension, insomnia, anticholinergic symptoms and weight gain.

Benzodiazepines

These are a group of medications that increase the activity of the GABA neurotransmitter system. These help in making people quiet and calm by reducing excess of excitement and anxiety. Still they are not considered to be the first choice of therapy because of the risks associated with their chronic use³⁰. The benzodiazepines most commonly used to treat anxiety disorders are clonazepam, alprazolam and lorazepam. These drugs work by facilitating GABA neurotransmission. In certain cases high dosage may lead to generation of side effects, hence, cognitive behavioural therapy is combined with low doses of benzodiazepine³¹. Common side effects include drowsiness, sedation, dizziness and loss of balance.

Other medications

Some of the evidences suggest that buspirone is effective in the treatment of generalised anxiety disorder. It works mainly through the serotonin neurotransmitter system and becomes effective within two to three weeks. Anti psychotic medications are rarely used to treat anxiety disorders. They are generally given at a low dose in combination with anti depressants.

Advancement and future scope of research in anxiety

Research on anxiety has provided a lot of useful information about the role of genetics and environmental influences. Although there are numerous treatment options available, they target

different symptoms of anxiety. In the last five years, most of the researches have been carried out on panic disorder. The findings include support for the usefulness of imipramine and clomipramine and probably other agents; evidence that the benzodiazepines alprazolam, diazepam, lorazepam, and clonazepam are approximately equally effective as antipanic agents; and high variability in relapse rates after discontinuation of drug treatment. Researchers are still trying to develop new ways of treating anxiety disorders and to improve the existing treatment methods. In the future, more effective and perhaps hybrid treatments of several options need to be explored in order to increase the success and duration of anxiety relief.

CONCLUSION

Epidemiological research suggests that anxiety disorders have the highest prevalence rate among psychiatric disorders. Anxiety disorders are treatable. Even though several types of treatment options are available for anxiety disorder still, more work needs to be directed toward merging of our knowledge of the biological mechanisms of anxiety with treatment in order to more accurately predict and improve treatment response.

REFERENCE

1. Spinella M. The Psychopharmacology of Herbal Medicine: Plant Drugs That Alter Mind, Brain and Behaviour. Cambridge, MA: The MIT press. J Psychiatry Neurosci. 2003 Jul; 28(4): 300–301.
2. Seligman, Walker EF, Rosenhan DL. Abnormal psychology. 4th Edition. New York: WW Norton & Company. 2001, chapter 7.
3. Eisenberg DM, Davis RB, Ettner SL. Trends in alternative medicine use in the United States. The Journal of the American Medical Association. 1998 ;280(18):1569-1575.
4. Wittchen HU, Jacobi F. Size and burden of mental disorders in Europe: a critical review and appraisal of 27 studies. Eur. Neuropsychopharmacol. 2005; 15:357-376.
5. Cates M, Wells BG. Anxiety Disorders. Textbook of Therapeutics: Drug and Disease Management. 1996: 1073-1093.
6. Pies RW. Clinical manual of psychiatric diagnoses and treatment: a biopsychosocial approach. American Psychiatric Press, Washington, DC; Prim Care Companion J Clin Psychiatry. 1999; 1(5): 166.
7. Hettema JM, Neale MC, Kendler KS. A review and meta analysis of the genetic epidemiology of anxiety disorders. Am J Psychiatry. 2001; 158(10):1568-78.
8. Torgersen S. Genetic Factors in Anxiety Disorders. Archives of General Psychiatry, 1983;40(10): 1085-1089.
9. Tocchetto A, Salum GA. Evidence of association between Val66Met polymorphism at BDNF gene and anxiety disorders in a community sample of children and adolescents. Sep 2011;502(3): 197–200.
10. Sandford J J, Argyropoulos SV, Nutt DJ. The psychobiology of anxiolytic drugs Part 1: basic neurobiology. Pharmacology & Therapeutics. 2000;88: 197-212.
11. Eysenck MW. Approaches to Abnormality. In MW Eysenck, Psychology: An International Perspective. New York: Psychology Press. 2004: 794-853.
12. Sarason IG, Sarason BR. The problem of maladaptive behavior. Abnormal Psychology. 8th Edition. New Delhi: Prentice Hall of India; 2000: 180-207.
13. Providing best care for anxiety disorders in general practice. NPS Prescribing Practice Review. NPS MedicineWise; 2009.
14. Barbotte E, Guillemin F, Chan N. Prevalence of impairments, disabilities, handicaps and quality of life in the general population: a review of recent literature. The International Journal of Public Health. 2001;79: 1047-1055.
15. Majcher D, Pollack MH. Childhood anxiety disorders: Do they grow out of it? Long-term outcomes of childhood disorders. Washington, DC: American Psychiatric Press. 1996: 139-169.
16. Offord DR, Boyle MH, Campbell D, Goering P, Lin E, Wong M et al. One-year prevalence of psychiatric disorder in Ontarians 15 to 64 years of age. Can Journal of Psychiatry 1996;41:559-563.
17. Eaton WW, Kessler RC, Wittchen HU, Magee WJ. Panic and panic disorder in the United States. Am J Psychiatry. 1994;151:413-420.
18. Lepine JP. The epidemiology of anxiety disorders: prevalence and societal costs. Journal of Clinical Psychiatry. 2002;14, 14-18.
19. Lisa B, Rivas-Vazquez, Rafael A. Assessment and treatment of social anxiety disorder. Professional Psychology: Research and Practice. 2003: 396-405.
20. Whittall ML, Thordarson DS, McLean PD. Treatment of obsessive-compulsive disorder: cognitive behavior therapy vs. exposure and response prevention. 2005;43(12):1559-76.
21. James D Herbert, Brandon A. Cognitive behavior therapy for generalized social anxiety disorder in adolescents: A randomized controlled trial. Journal of Anxiety Disorders. 2009: 167–177.
22. Knekt P, Lindfors O, Laaksonen MA. Psycho-therapy Study Group. Effectiveness of short-term and long-term psychotherapy on work ability and functional capacity: A randomized clinical trial on depressive and anxiety disorders. Journal of Affective Disorders. 2008;107(1-3): 95-106.
23. Feldman. American Psychological Association. 2004.
24. Snyder BD, Polasek TM, Doogue MP. Drug interactions: principles and practice. AustPrescr 2012;35:85-88.
25. Cassano, Giovanni B, Rossi, Nicolò Baldini. Psychopharmacology of anxiety disorders. Dialogues in Clinical Neuroscience. 2002;4(3): 271–285.
26. Barlow, David H, Durand, Mark V. Mood Disorders and Suicide. Abnormal Psychology: An Integrative Approach. 2009;239.
27. Koen N, Stein DJ. Pharmacotherapy of anxiety disorders: A critical review. Dialogues ClinNeurosci. 2011;13(4):423–437.
28. Ravindran LN, Stein MB. The pharmacologic treatment of anxiety disorders: A review of progress. J Clin Psychiatry. 2010;71(7): 839–854.

29. Llorca PM, Spadone C, Sol O. Efficacy and safety of hydroxyzine in the treatment of generalized anxiety disorder: a 3-month double-blind study. *J Clin Psychiatry*. 2002, November; 63 (11): 1020–1027.
30. McDougle CJ. Update on pharmacologic management of OCD: Agents and augmentation. *J Clin Psychiatry*. 1997;58:11–17.
31. Ravindran LN, Stein MB. The pharmacologic treatment of anxiety disorders: A review of progress. *J Clin Psychiatry*.