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Anxiety: Causes and Management

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Anxiety disorders affect one-eighth of the total population worldwide, and have become a very important area of research interest in psychopharmacology. People with anxiety disorders can benefit from psychological treatments, pharmacotherapy or a combination of the two. Common limitations of conventional antianxiety therapy include co-morbid psychiatric disorders and increase in dose of drugs leading to intolerable side effects. These limitations have prompted the use of traditional and alternative systems of medicine. This paper reviews the causes, and the effective and safe therapy for anxiety disorders.

***Keywords**:* anxiety disorders, psychological treatments, pharmacotherapy, alternative therapy.

The environment we are living in is physically, mentally, emotionally, socially and morally dynamic and challenging. We possess effective mechanisms to meet every day stress. Sometimes, normal adaptive mechanisms can be over-activated and, thus, become maladaptive. A common outcome of such over-activation is anxiety and insomnia (Spinella, 2001).

Anxiety is a subjective feeling of unease, discomfort, apprehension or fearful concern accompanied by a host of autonomic and somatic manifestations. Anxiety is a normal, emotional, reasonable and expected response to real or potential danger. However, if the symptoms of anxiety are prolonged, irrational, disproportionate and/or severe; occur in the absence of stressful events or stimuli; or interfere with everyday activities, then, these are called Anxiety Disorders (DSM IV-TR, 2000).

Anxiety disorders are among the most common mental, emotional, and behavioral problems (Kessler et al., 2005a, 2005b; Olatunji et al., 2007; Kessler & Wang, 2008). These affect one-eighth of the total population worldwide, and have become a very important area of research interest in psychopharmacology (Eisenberg et al., 1998; Dopheide & Park, 2002; WHO, 2004).

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In addition to the high prevalence, anxiety disorders account for major expenditure for their management (DuPont et al., 1996); and anxiety disorders have a substantial negative impact on quality of life (Gladis et al., 1999; Mendlowicz & Stein, 2000; Olatunji et al., 2007).

Symptoms of Anxiety Disorders

The subjective experience of anxiety typically has two components namely physical component and emotional component which affect the cognitive processes of the individual (Cates et al., 1996; Charles and Shelton, 2004; Augustin, 2005; Shri, 2006; Rang et al., 2007) and these have been shown in Figure 1.

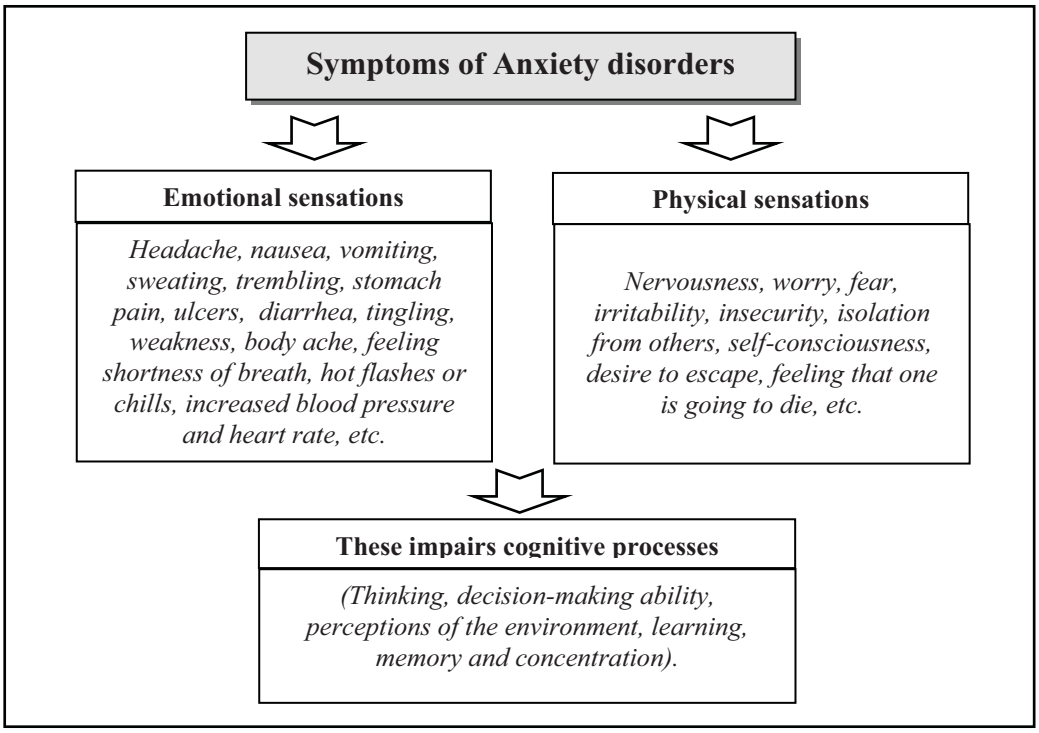

Figure 1. Symptoms of anxiety.

Etiology

Anxiety disorders are among the most frequent mental disorders encountered in clinical practice (Kirkwood & Melton, 2002). These represent a heterogenous group of disorders, probably with no single unifying etiology. Various psychodynamic, psychoanalytic, behavioral, cognitive, genetic and biological theories have been proposed to explain the etiology and pathophysiology of anxiety disorders (Cates et al., 1996). These are said to be BioPsychoSocial factors that contribute to anxiety disorders (Pies, 1994; White, 2005; Wong, 2006). Table 1 shows the bifurcation of the factors.

Table 1

Etiology of Anxiety Disorders

Biological causes	**Psychological causes**	**Social causes**
• Heredity • Neurotransmitter imbalance • Illness • Medications • Nutritional factors	• Personality traits • Low self-esteem • Cognitive dissonance • Negative emotions • Inter and/or intra-personal conflicts • Developmental crises • Perception of situational factors	• Adverse Life Experiences • Lack of social support • Work stress • Lack of social skills • Changing values • Conflict of societal norms • Terrorism • Natural calamities

Biological factors

Genetic factors

Genetic factors predispose certain people to anxiety disorders. There is a higher chance of an anxiety disorder in the parents, children and siblings of a person with an anxiety disorder than in the relatives of someone without an anxiety disorder (Torgersen, 1983; Weissman, 1993; Goldman, 2001).

Neurotransmitter imbalance

Brain imaging and functional studies have shown that several neurotransmitters are linked to the neurobiology of anxiety (Cates et al., 1996; Sandford et al., 2000; Millan, 2003; Augustin, 2005). The diagrammatic representation of this has been shown in Figure 2.

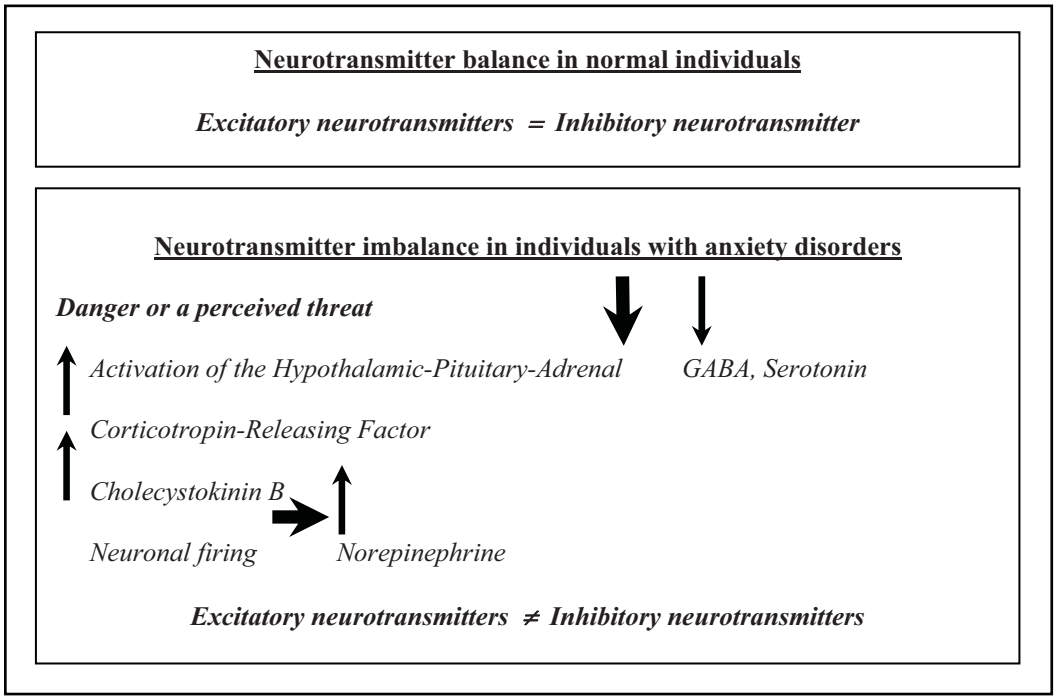

Figure 2. Neurotransmitters involved in occurrence of anxiety disorders.

Psychological factors

Anxiety can result when a combination of increased internal and external stresses overwhelm one's normal coping abilities or when one's ability to cope normally is lessened for some reason. The psychological factors are summarized below:

- Psychodynamic: When internal competing mental processes, instincts and impulses conflict, causing distress.
- Behavioral: Anxiety is a maladaptive learned response to specific past experiences and situations that become generalized to future similar situations.

- Spiritual: When people experience a profound, unquenchable emptiness and nothingness to their lives, often leading to distress concerning their mortality and eventual death (Sarason & Sarason, 2000; Brannon & Feist, 2004).

Social factors

Life experiences like death in the family, divorce, job loss, financial loss, accident or major illness affect a person's attitude and response to life situations. Long term exposure to abuse, violence, terrorism and poverty may affect an individual's susceptibility to anxiety disorders (Eysenck, 2004).

Types of Anxiety Disorders

Anxiety disorders can be classified into several categories (ICD-10, 1992; Cates et al*.,* 1996; DSM-IV-TR, 2000; Augustin, 2005; Rang et al*.,* 2007). As shown in table 2 the different types of anxiety disorders and their clinical symptoms can be differentiated.

Table 2

Type of Anxiety Disorders and Their Clinical Symptoms

Anxiety disorder	Clinical Symptoms
Generalized anxiety disorder	Excessive and unrealistic worry that is difficult to control about several life circumstances for 6 months or longer
Panic disorder (With/without agoraphobia)	Occurrence of recurrent, unexpected attacks of overwhelming fear occurring in association with marked somatic symptoms, such as sweating, tachycardia, chest pains, trembling, choking, etc.

(continued)

Table 2 (continued)

Anxiety disorder	Clinical Symptoms
Agoraphobia without history of panic disorder	Irrational and often disabling fear of public places or open areas
Phobic disorders • Social phobia • Specific phobias	Strong fears of specific things or situations, e.g., snake, open spaces, flying, social interactions, etc.
Post-traumatic stress disorder	Anxiety triggered by insistent recall of past stressful/traumatic experiences
Separation anxiety disorder	Difficulty in leaving dear ones
Obsessive-compulsive disorder	When one is trapped in a pattern of repetitive thoughts and behaviors, i.e. recurrent obsessions or compulsions that cause marked distress; are time consuming; or interfere significantly with normal occupational functioning, social activities, or relationships
Acute stress disorder	Anxiety reaction which may occur shortly after traumatic exposure
Anxiety disorder due to a general medical condition	Knowledge that one has chronic and perhaps disabling medical illness can precipitate anxiety
Substance induced anxiety disorder	Anxiety related to substance abuse
Anxiety disorder not otherwise specified	Anxiety reactions which do not fall in any of above categories

Occurrence and Epidemiology

About 500 million people, world wide, suffer from mental and behavioral disorders (Barbotte et al*.,* 2001). Five of the ten leading causes of disability and premature death worldwide are psychiatric conditions. Mental disorders represent not only an immense psychological, social and economic burden to society, but also increase the risk of physical illnesses. Neuropsychiatric conditions account for 13% of the total Disability Adjusted Life Years (DALYs) lost due to all diseases and injuries in the world and are estimated to increase to 15% by the year 2020 (WHO, 2004).

Anxiety disorders, like depression, are among the most prevalent psychiatric disorders. They comprise a wide range of different disorders. Most anxiety disorders first appear during childhood and adolescence. Evidence shows that a high proportion of children do not grow out of their anxiety disorders during adolescence and adulthood (Majcher & Pollack, 1996; Murray & Lopez, 1996). Different surveys suggest that anxiety affects one-eighth of the total population of the world. The lifetime overall prevalence rate for anxiety disorders is 24.9%. This data suggests anxiety disorders are more chronic than affective or substance abuse disorders (Cates et al., 1996). Prevalence of anxiety disorders is difficult to pinpoint since even small changes in diagnostic criteria, interview tools, or study methodology affect results. World wide prevalence of different types of anxiety disorders varies (Cates et al., 1996) and have been shown in table 3.

Table 3

World Wide Prevalence of Anxiety Disorders

Anxiety Disorder	**Prevalence**	**Comments**
Panic	5 % in women 2 % in men	More prevalent in women High comorbidity rate with major depression
Generalized anxiety disorder	5.1 %	More frequent in females Likely to be comorbid with other disorders
Obsessive-compulsive disorder	2.3 %	Equally common in men and women. First symptoms very often observed in children
Post traumatic stress disorder	1% in general population 30-50% in traumatized Populations	Women are more likely to be afflicted. Rape is the most likely trigger
Social phobia	13.3 %	More common in women than men

There are certain medical conditions, as shown in table 4, the symptoms of which resemble the symptoms of anxiety disorders (e.g., palpitations, tachycardia, chest pain or tightness, shortness of breath, hyperventilation) and, thus, make it difficult to identify anxiety disorders (Kirkwood & Melton, 2002; Augustin, 2005).

Table 4

Some Medical Diseases With Anxiety-Like Symptoms

Cardiovascular	*Angina, arrhythmias, congestive heart failure, myocardial infarction, supraventricular tachycardia, mitral valve prolapse*
Endocrine and metabolic	*Hyperthyroidism, hypoglycemia, Addison's disease, Cushing's disease, pheochromocytoma, electrolyte abnormalities, hyperkalemia*
Neurological	*CNS tumors, dementia, migraine, pain, Parkinson's disease, seizures, stroke, multiple sclerosis, vertigo*
Respiratory system	*Asthma, pulmonary edema, embolus, pneumonia, chronic obstructive lung disease*
Gastrointestinal	*Crohn's disease, ulcerative colitis, irritable bowel syndrome*
Others	*HIV, systemic lupus erythematosus, anemias*

Most psychiatric patients will have two or more concurrent psychiatric diseases (co-morbidity) within their lifetime. Anxiety may be a concomitant symptom of several major psychiatric diseases. Anxiety symptoms are extremely common in patients with mood disorders, schizophrenia, delirium, dementia, and substance use disorders (Kirkwood & Melton, 2002).

There are different classes of drugs that cause anxiety like symptoms (Cates et al., 1996; Kirkwood & Melton, 2002; Augustin, 2005), and have been tabulated in table 5.

Table 5

Different Classes of Drugs That Cause Anxiety Like Symptoms

CNS stimulants	*Amphetamines, caffeine, cocaine, ephedrine, methylphenidate*
CNS depressant withdrawal	*Alcohol, anxiolytics, barbiturates, narcotic agonists, sedative-hypnotics*
Cardiovascular drugs	*Captopril, enalapril, digoxin, reserpine, hydralazine*
Others	*Anticholinergics, anticonvulsants, antihistamines, antidepressants, antipsychotics, bronchodilators, NSAIDS, steroids, thyroid preparations*

Management of Anxiety

Anxiety disorders are the most prevalent of psychiatric disorders, yet less than 30% of individuals who suffer from anxiety disorders seek treatment (Lepine, 2002). People with anxiety disorders can benefit from a variety of treatments and services. Following an accurate diagnosis, possible treatments include (Barlow, 2001; NIMH, 2006) psychological treatments and mediation.

Psychological treatments

Psychotherapy is almost always the *treatment of choice* except in cases where anxiety is so severe that immediate relief is necessary to restore functioning and to prevent immediate and severe consequences. This includes the following:

- ***Behavioral therapies:*** These focus on using techniques such as guided imagery, relaxation training, biofeedback (to control stress and muscle tension); progressive desensitization, flooding as means to reduce anxiety responses or eliminate specific phobias. The person is gradually exposed to the object or situation that is feared. At first, the exposure may be only through pictures or audiotapes. Later, if possible, the person actually confronts the feared object or situation. Often the therapist will accompany him or her to provide support and guidance.

- ***Cognitive-behavioral therapy (CBT):*** In this therapy, people learn to deal with fears by modifying the ways they think and behave. A major aim of CBT and behavioral therapy is to reduce anxiety by eliminating beliefs or behaviors that help to maintain the anxiety disorder. Research has shown that CBT is effective for several anxiety disorders, particularly panic disorder and social phobia (Herbert et al., 2009). It has *two* components. The *cognitive component* helps people change thinking patterns that keep them from overcoming their fears. The *behavioral component* of CBT seeks to change people's reactions to anxiety-provoking situations. A key element of this component is exposure, in which people confront the things they fear, i.e., CBT addresses underlying "automatic" thoughts and feelings that result from fear, as well as specific techniques to reduce or replace maladaptive behavior patterns.

- ***Psychotherapy:*** Psychotherapy centers on resolution of conflicts and stresses, as well as the developmental aspects of anxiety disorders solely through talk therapy. Psychotherapy involves talking with a trained mental health professional, such as a psychiatrist, psychologist, social worker, or counselor to learn how to deal with problems like anxiety disorders (Knekt et al., 2008).

- ***Psychodynamic therapy:*** This therapy**,** first suggested by Freud, is based on the premise that primary sources of abnormal behavior are unresolved past conflicts and the possibility that unacceptable unconscious impulses will enter consciousness.

- ***Family therapy and parent training:*** Here the focus is on the family and its dynamics. This is based on the assumption that the individuals of a family cannot improve without understanding the conflicts that are to be found in the interactions of the family members. Thus, each member is expected to contribute to the resolution of the problem being addressed (American Psychological Association, 2004; Feldman, 2004).

Table 6

Major Classes of Medications Used for Various Anxiety Disorders

Class	Generic name	Used for	Mechanism of action	Advantages	Limitations
Anti-convulsants	Gabapentin	SAD	Affect GABA	Usually effective within 2-4 weeks	Sedation
Azaspirones	Buspirone	GAD	Enhances the activity of serotonin	Less sedating than benzodiaze-pines	Works slowly
Benzo-diazepines	Lorazepam Clonazepam Oxazepam Diazepam Alprazolam	GAD, SAD, Panic disorder	Enhance the function of GABA	Fast-acting, some people feel better the first day	Potentially habit-forming, can cause drowsiness, can produce withdrawal symptoms, discontinuation should be done slowly
Beta blockers	Propanolol Atenolol	SAD	Reduce ability to produce adrenaline	Fast acting; not habit-forming	Should not be used with pre-existing medical conditions, such as asthma, congestive heart failure, diabetes, vascular disease, hypothyroidism and angina pectoris
Monoamine oxidase inhibitors (MAOIs)	Selegilene Isocarboxid Phenelzine Tranylcypromine	Panic disorder, SAD, PTSD	Block the effect of an important brain enzyme, preventing the breakdown of serotonin and noradrenaline	Effective for many people, especially for patients not responding to other medications, 2-6 weeks until improvement occurs	Strict dietary restrictions and potential drug interactions, changes in blood pressure, moderate weight gain, reduced sexual response, insomnia
Selective serotonin reuptake inhibitors (SSRIs)	Citalopram Fluvoxamine Paroxetine Fluoxetine Sertraline	Panic disorder, OCD, SAD, GAD	Affect the concentration of serotonin	Effective, with fewer side effects than other medications. 4-6 weeks until improvement occurs	Some people experience nausea, nervousness and diminished sex drive
Tricyclic antidepressants (TCAs)	Nortriptyline Amitriptyline Imipramine	Panic disorder, PTSD, OCD	Regulates serotonin and/or noradrenaline in the brain	Effective for many people, may take 2-6 weeks until improvement occurs.	Dry mouth, constipation, blurry vision, difficulty urinating, dizziness, low blood pressure, moderate weight gain, sexual side effects

Note. GAD = Generalized anxiety disorder, OCD = Obsessive compulsive disorder, PTSD = Post Traumatic stress disorder, SAD=Social anxiety disorder .

Alternative treatments for anxiety disorders

Complementary and alternative medicine (CAM) plays a significant role in health care systems. CAM therapies have increasingly attracted the attention of medical doctors and researchers as well as the public, the government, and the media. Between 1990 and 1997, the number of consumers using CAM therapies rose significantly, from 33.8% to 42.1% (Ernst, 2006). Patients with chronic pain conditions, including arthritis, chronic neck and backache, headache, digestive

problems and mental health conditions (including insomnia, depression, and anxiety) were high users of CAM therapies (Cauffeild, 2000; Kessler et al., 2001; Elkins et al., 2005; Saeed et al., 2007). These disorders are not easily treated with conventional medical therapies (Figure 2). Of the reported cases of anxiety, more than 40% patients use CAM.

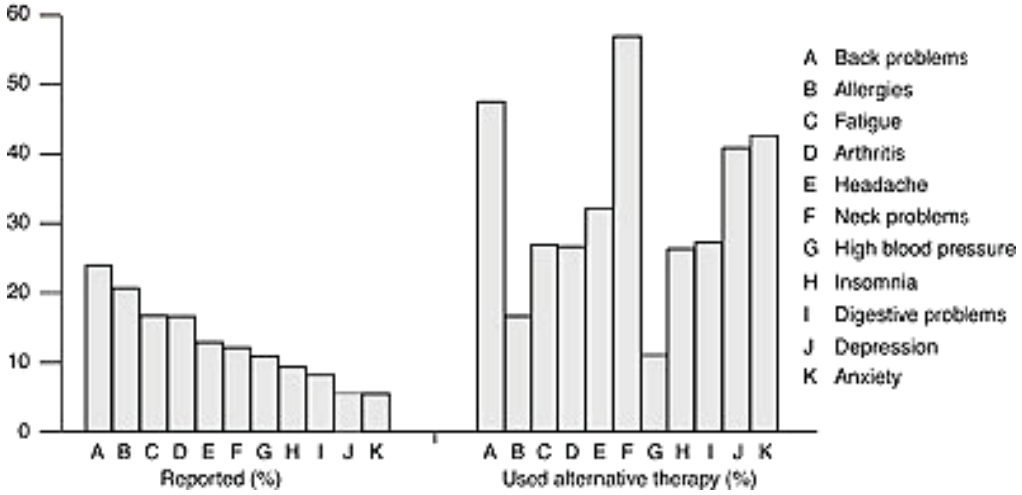

Figure 2. Disorders for which CAM is used.

There are different types of CAMs that are used for the management of anxiety (Kessler et al., 2001; Moquin et al., 2009; NIH, 2009). The most common therapies included relaxation techniques, herbal medicines, massage, chiropractic, spiritual healing by others, and nutritional supplements (Figure 3). In particular, the use of herbal remedies and nutritional supplements rose 380% and 130%, respectively, between 1990 and 1997. These are shown in table 7.

Table 7

Complimentary and Alternate Therapies for Treatment of Anxiety

Cognitive feedback	Oral medication	Physical treatments	Alternate medical systems	Other therapies
a) Relaxation techniques	a) Herbal medicine	a) Yoga	a) Aromatherapy	a) Spiritual healing
b) Imagery	b) Megavitamins	b) Acupuncture	b) Ayurveda	b) Dietary modifications
c) Self-help group	c) Lycopene	c) Physiotherapy	c) Traditional Chinese medicine	c) Energy healing (e.g., Reiki)
d) Biofeedback	d) Zinc	d) Tai Chi	d) Homeopathy	d) Laughter therapy
e) Hypnotherapy	e) Omega-3-fatty acids	e) Chiropractice	e) Naturopathy	e) Lifestyle intervention programmes

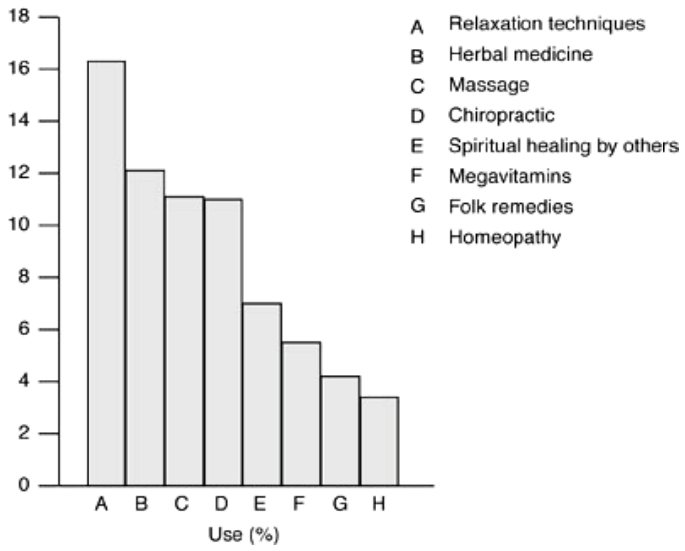

Figure 3. Commonly used CAM therapies for management of anxiety.

Common limitations of antianxiety drug therapy include co-morbid psychiatric disorders (Regier et al., 1998) and increase in dose leading to intolerable side effects (Cates et al., 1996). These limitations have prompted scientists to investigate plants which are commonly employed in traditional and alternative systems of medicine for sleep disorders and related diseases with a view to find safer drugs (Spinella, 2001; Chung et al., 2005; Kumar, 2006).

Plants used for management of anxiety

The World Health Organisation estimates that 80% of the world population relies on herbal medicine (Eisenberg et al., 1998). Various plants have been investigated for their anxiolytic effects (Carlini, 2003) and many have shown marked antianxiety activity. Monoherbal preparations containing *Scutellaria laterifolia, Centella asiatica, Paullinia cupana, Piper methysticum, Bacopa monniera, Cymbopogan citratus, Passiflofa incarnata* and *Valeriana officinalis* were subjected to randomised clinical trials to study their effect in alleviation of anxiety (Ernst, 2006). According to the reported data, *Piper methysticum* (Pittler et al., 2002) and *Bacopa monniera*, (Stough et al., 2001) are associated with anxiolytic activity in humans. In another trial on generalized anxiety disorder (GAD) in hospital based clinical set-up, *Ocimumn sanctum* significantly attenuated generalized anxiety disorders and also attenuated its correlated stress and depression (Bhattacharyya et al., 2008).

Conclusion

Epidemiological research suggests that anxiety disorders have the highest prevalence rate among psychiatric disorders. Conventional pharmacotherapy is limited by side effects such as psychomotor impairment, potentiation of other central depressant drugs and dependence liability. Hence, complementary and alternative medicine and plant-derived medications are being investigated as potential anxiolytic agents.

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