Therapeutic measures for generalized anxiety disorder

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Abstract
Generalized anxiety disorder (GAD) is an anxiety disorder characterized by excessive, uncontrollable and often irrational worry, that is, apprehensive expectation about events or activities. Generalized anxiety disorder is based on psychological components that include cognitive avoidance, worry beliefs, ineffective problem-solving and emotional processing, interpersonal issues, previous trauma, intolerance of uncertainty, negative problem orientation, ineffective coping, emotional hyper-arousal, poor understanding of emotions, negative cognitive reactions to emotions, maladaptive emotion management and regulation, experiential avoidance, and behavioral restriction, (Behr et.al 2009).
To combat the previous cognitive and emotional aspects of GAD, psychologists often include some of the following key treatment components in their intervention plan; self-monitoring, relaxation techniques, self-control desensitization, gradual stimulus control, cognitive restructuring, worry outcome monitoring, present-moment focus, expectancy-free living, problem-solving techniques, processing of core fears, socialization, discussion and reframing of worry beliefs, emotional skills training, experiential exposure, psycho-education, mindfulness and acceptance exercises.
Recently focus is increasing on prevention of GAD. Avoidance of caffeine may prevent GAD. Additionally, avoiding nicotine decreases the risk for the development of anxiety disorders including generalized anxiety disorder (Bruce and Lader, 2009). Cognitive behavioral therapy (CBT) is more effective in the long term than medications. While both treatments reduce anxiety, CBT is more effective in reducing depression. However, the overall outcomes differed but this difference was not found to be statistically significant.
Thus there are behavioral, cognitive, and a combination of both treatments for GAD that focus on some of those key components. With appropriate integration of various therapeutic measures, the outlook for the generalized anxiety disorders is encouraging. In addition, it is important to differentiate between short-term and long-term results. Even through the results of therapy are often difficult to assess, it would appear that the great majority of patients, 90 percent or more can benefit substantially from appropriate help. In many cases, the use of periodic “booster treatments” can probably improve long range results.

Keywords: Generalized anxiety disorder (GAD), Cognitive, Behavioral, Therapeutic measures, Booster-treatment.

1. Introduction
Generalized anxiety disorder (GAD) is an anxiety disorder characterized by excessive, uncontrollable and often irrational worry, that is, apprehensive expectation about events or activities. This excessive worry often interferes with daily functioning, as individuals with GAD typically anticipate disaster, and are overly concerned about everyday matters such as health issues, money, death, family problems, friendship problems, interpersonal relationship problems, or work difficulties, (Torpy, Janet and Burke, 2011) [3]. Individuals often exhibit a variety of physical symptoms, including fatigue, fidgeting, headaches, nausea, numbness in hands and feet, muscle tension, muscle aches, difficulty swallowing, excessive stomach acid buildup, stomach pain, vomiting, diarrhea, bouts of breathing difficulty, difficulty concentrating, trembling, twitching, irritability, agitation, sweating, restlessness, insomnia, hot flashes, rashes, and inability to fully control the anxiety.
These symptoms must be consistent and ongoing, persisting at least six months, for a formal diagnosis of GAD. Once GAD develops, it may become chronic, but can be managed or eliminated with proper treatment, (Rickels and Schweizer, 1990) [8].

DSM Criteria to Diagnose General Anxiety Disorder (GAD)
The diagnostic criteria for GAD as defined by the Diagnostic and Statistical Manual of Mental Disorders DSM-5 (2013), published by the American Psychiatric Association, are as follows:
A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).
B. The individual finds it difficult to control the worry.
C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 months):
   1. Restlessness or feeling keyed up or on edge.
   2. Being easily fatigued.
   3. Difficulty concentrating or mind going blank.
   4. Irritability.
   5. Muscle tension.
   6. Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep).
D. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism).
F. The disturbance is not better explained by another mental disorder (e.g., anxiety or worry about having panic attacks in panic disorder, negative evaluation in social anxiety disorder, social phobia, contamination or other obsessions in obsessive-compulsive disorder, separation from attachment figures in separation anxiety disorder, reminders of traumatic events in posttraumatic stress disorder, gaining weight in anorexia nervosa, physical complaints in somatic symptom disorder, perceived appearance flaws in body dysmorphic disorder, having a serious illness in illness anxiety disorder, or the content of delusional beliefs in schizophrenia or delusional disorder).

**Therapeutic Measures for Generalized Anxiety Disorder**

Recently focus is increasing on prevention of mental disorders. Avoidance of caffeine may prevent GAD. Additionally, avoiding nicotine decreases the risk for the development of panic disorder, negative evaluation in social anxiety disorder, social phobia, contamination or other obsessions in obsessive-compulsive disorder, separation from attachment figures in separation anxiety disorder, reminders of traumatic events in posttraumatic stress disorder, gaining weight in anorexia nervosa, physical complaints in somatic symptom disorder, perceived appearance flaws in body dysmorphic disorder, having a serious illness in illness anxiety disorder, or the content of delusional beliefs in schizophrenia or delusional disorder.

Cognitive behavioral therapy (CBT) is more effective in the long term than medications (such as SSRIs), and while both treatments reduce anxiety, CBT is more effective in reducing depression; however, while the overall outcomes differed, this difference was not found to be statistically significant.

Generalized anxiety disorder is based on psychological components that include cognitive avoidance, positive worry beliefs, ineffective problem-solving and emotional processing, interpersonal issues, previous trauma, intolerance of uncertainty, negative problem orientation, ineffective coping, emotional hyperarousal, poor understanding of emotions, negative cognitive reactions to emotions, maladaptive emotion management and regulation, experiential avoidance, and behavioral restriction, (Behr et. al). To combat the previous cognitive and emotional aspects of GAD, psychologists often include some of the following key treatment components in their intervention plan; self-monitoring, relaxation techniques, self-control desensitization, gradual stimulus control, cognitive restructuring, worry outcome monitoring, present-moment focus, expectancy-free living, problem-solving techniques, processing of core fears, socialization, discussion and reframing of worry beliefs, emotional skills training, experiential exposure, psychoeducation, mindfulness and acceptance exercises. There exist behavioral, cognitive, and a combination of both treatments for GAD that focus on some of those key components.

The cognitive–behavioral orientated psychotherapies include the two main treatments are cognitive behavioral therapy and acceptance and commitment therapy. Intolerance of uncertainty therapy and motivational interviewing are two new treatments for GAD that are used as either stand-alone treatments or additional strategies that may enhance CBT, (Hoyer and Jurgen, 2011) [27].

**Cognitive behavioral therapy**

Cognitive behavioral therapy (CBT) is a psychological method of treatment for GAD that involves a therapist working with the patient to understand how thoughts and feelings influence behavior. The goal of the therapy is to change negative thought patterns that lead to the patient's anxiety, replacing them with positive, more realistic ones. Elements of the therapy include exposure strategies to allow the patient to confront their anxieties gradually and feel more comfortable in anxiety-provoking situations, as well as to practice the skills they have learned. CBT can be used alone or in conjunction with medication.

Components of Cognitive Behavioral Therapy (CBT) for generalized anxiety disorders includes:

1. **Psychoeducation,**
2. **Self-monitoring,**
3. **Stimulus control techniques,**
4. **Relaxation,**
5. **Self-control desensitization,**
6. **Cognitive restructuring,**
7. **Worry exposure,**
8. **Worry behavior modification,** and
9. **Problem-solving.**
8. Worry behavior prevention requires patients to monitor the behaviors that caused them worry and are then asked to prevent themselves from engaging in them. Instead they are encouraged to use other coping mechanisms learned earlier in the treatment.

9. Problem solving focuses on dealing with current problems through a problem-solving approach: (1) definition of the problem, (2) formulation of goals, (3) creation of alternative solutions, (4) decision-making, and (5) implementing and verifying the solutions, (Hozer, Jurgen, 2011) [27].

There is little debate regarding the effectiveness of CBT for GAD. However, there is still room for improvement because only about 50% of those who complete treatments achieve higher functioning or recovery after treatment. Therefore, there's a need for enhancement of current components of CBT. CBT usually helps one third of the patients substantially, whilst another third does not respond at all to treatment, (Barlow, 2007).

**Acceptance and commitment therapy**

Acceptance and commitment therapy (ACT) is a behavioral treatment based on acceptance-based models. ACT is designed with the purpose to target three therapeutic goals: (1) reduce the use of avoiding strategies intended to avoid feelings, thoughts, memories, and sensations; (2) decreasing a person's literal response to their thoughts (e.g., understanding that thinking "I'm hopeless" does not mean that the person's life is truly hopeless), and (3) increasing the person's ability to keep commitments to changing their behaviors. These goals are attained by switching the person's attempt to control events to working towards changing their behavior and focusing on valued directions and goals in their lives as well as committing to behaviors that help the individual accomplish those personal goals, (Roemer Lizabeth, 2006) [31]. This psychological therapy teaches mindfulness (paying attention on purpose, in the present, and in a nonjudgmental manner) and acceptance (openness and willingness to sustain contact) skills for responding to uncontrollable events and therefore manifesting behaviors that enact personal values, (Smout, 2012) [32]. Like many other psychological therapies, ACT works best in combination with pharmacology treatments.

**Intolerance of uncertainty therapy**

Intolerance of uncertainty therapy (IUT) refers to a consistent negative reaction to uncertain and ambiguous events regardless of their likelihood of occurrence. IUT is used as a stand-alone treatment for GAD patients. Thus, IUT focuses on helping patients in developing the ability to tolerate, cope with and accept uncertainty in their life in order to reduce anxiety. IUT is based on the psychological components of psychoeducation, awareness of worry, problem-solving training, re-evaluation of the usefulness of worry, imagining virtual exposure, recognition of uncertainty, and behavioral exposure. Studies have shown support for the efficacy of this therapy with GAD patients with continued improvements in follow-up periods.

**Motivational interviewing**

According to Hozer and Jurgen, 2011, promising innovative approach to improving recovery rates for the treatment of GAD is to combine CBT with Motivational Interviewing (MI). Motivational Interviewing is a strategy centered on the patient that aims to increase intrinsic motivation and decrease ambivalence about change due to the treatment. MI contains four key elements; (1) express empathy, (2) heighten dissonance between behaviors that are not desired and values that are not consistent with those behaviors, (3) move with resistance rather than direct confrontation, and (4) encourage self-efficacy. It is based on asking open-ended questions and listening carefully and reflectively to patients' answers, eliciting "change talk", and talking with patients about the pros and cons of change. Some studies have shown the combination of CBT with MI more efficient than CBT alone.

**Medications**

**Selective serotonin reuptake inhibitors**

Pharmaceutical treatments for GAD include selective serotonin reuptake inhibitors (SSRIs). These are the first line of treatment. The two SSRI antidepressants approved by the FDA are Common side effects include nausea, sexual dysfunction, headache, diarrhea, constipation, restlessness, increased risk of suicide in young adults and adolescents, serotonin syndrome (caused by an overdose of the SSRI), among others, (Balwin and Pallanti, 2012) [33].

**Benzodiazepines**

Benzodiazepines are most often prescribed to patients with Generalized Anxiety Disorder. Research suggests that these drugs give some relief, at least in the short term. However, they carry some risks, mainly impairment of both cognitive and motor functioning, and psychological and physical dependence that makes it difficult for patients to stop taking them. It has been noted that people taking benzodiazepines are not as alert on their job or at school. Additionally, these drugs may impair driving and they are often associated with falls in the elderly, resulting in hip fractures. These shortcomings make the use of benzodiazepines optimal only for short-term relief of anxiety, (Barloo and Durand, 2009) [35]. CBT and medication are of comparable efficacy in the short-term but CBT has advantages over medication in the longer term, (Durham, 2007) [37].

Benzodiazepines (or "benzos") are fast-acting hypnotic sedatives that are also used to treat GAD and other anxiety disorders. Benzodiazepines are prescribed for generalized anxiety disorder and show beneficial effects in the short term. Popular Benzodiazepines for GAD include alprazolam, lorazepam and clonazepam. The World Council of Anxiety does not recommend the long-term use of benzodiazepines because they are associated with the development of tolerance, psychomotor impairment, cognitive and memory impairments, physical dependence and a withdrawal syndrome. Side effects include drowsiness, reduced motor coordination and problems with equilibrioception, (Swetwart Westra, 2002) [38].

**Pregabalin and gabapentin**

Pregabalin (Lyrica) acts on the voltage-dependent calcium channel to decrease the release of neurotransmitters such as glutamate, norepinephrine and substance P. Its therapeutic effect appears after 1 week of use and is similar in effectiveness to lorazepam, alprazolam and venlafaxine but pregabalin has demonstrated superiority by producing more consistent therapeutic effects for psychic and somatic anxiety symptoms. Long-term trials have shown continued effectiveness without the development of tolerance and additionally, unlike benzodiazepines, it does not disrupt sleep architecture and produces less severe cognitive and psychomotor impairment. It
also has a low potential for abuse and dependency and may be preferred over the benzodiazepines for these reasons. The anxiolytic effects of pregabalin appear rapidly after administration, similar to the benzodiazepines, which gives pregabalin an advantage over many anxiolytic medications such as antidepressants, (Wensel, Powe, 2012) [41]. Gabapentin (Neurontin), a closely related drug to pregabalin with the same mechanism of action, has also demonstrated effectiveness in the treatment of GAD, though unlike pregabalin, it has not been approved specifically for this indication. Nonetheless, it is likely to be of similar usefulness in the management of this condition, and by virtue of being off-patent, it has the advantage of being significantly less expensive in comparison. In accordance, gabapentin is frequently prescribed off-label to treat GAD, (John Reynolds, 2011) [44].

Psychiatric drugs
- 5-HT1A receptor partial agonists, such as buspirone (BuSpar) and tandospirone (Sediel).
- Serotonin-norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine (Effexor) and duloxetine (Cymbalta).
- Newer, atypical serotonin antidepressants, such as vilazodone (Viibryd), vortioxetine (Brintellix), and agomelatine (Valdoxan).
- Tricyclic antidepressants (TCAs), such as imipramine (Tofranil) and clomipramine (Anafranil).
- Certain monoamine oxidase inhibitors (MAOIs), such as moclobemide (Aurorix) and, rarely, phenelzine (Nardil).

Conclusion
With appropriate therapy-usually involving the integration of various therapeutic measures the outlook for the generalized anxiety disorders is encouraging. In addition, it is important to differentiate between short-term and long-term results but even through the results of therapy are often difficult to assess, it would appear that the great majority of patients, 90 percent or more can benefit substantially from appropriate help. In many cases, the use of periodic “booster treatments” can probably improve long range results.

References
4. International Classification of Diseases) ICD-10


