


TREATMENT OF GENERALIZED ANXIETY DISORDER: THERAPEUTIC APPROACHES AND CLINICAL CHALLENGES

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ABSTRACT

INTRODUCTION: Anxiety disorders represent a group of prevalent psychiatric conditions, with Generalized Anxiety Disorder (GAD) being one of the most common among adults. It is estimated that GAD affects approximately 3% to 6% of the global adult population, with a significant prevalence rate also observed in children and adolescents (DeGeorge, Grover, & Streeter, 2022). This chronic disorder is characterized by generalized, diffuse, and excessive anxiety that impairs various domains of the patient's life, such as social, familial, and professional and is often associated with somatic symptoms (Strawn et al., 2018). The clinical relevance of GAD is further highlighted by the fact that individuals with this disorder are more prone to developing comorbidities, such as depressive disorders and other anxiety disorders, as well as having an elevated lifetime risk of suicide (Strawn et al., 2018).

Keywords: Generalized Anxiety Disorder, Therapeutic Approaches, Clinical Challenges.

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INTRODUCTION

Anxiety disorders are a group of prevalent psychiatric conditions, with GAD being one of the most common among adults. GAD is estimated to affect approximately 3% to 6% of the global adult population, with a significant prevalence rate also observed in children and adolescents (DeGeorge, Grover, & Streeter, 2022). This chronic disorder is characterized by generalized, diffuse, and excessive anxiety that impairs various domains of the patient's life, such as social, familial, and professional and is often associated with somatic symptoms (Strawn et al., 2018). The clinical relevance of GAD is further highlighted by the fact that individuals with this disorder are more prone to developing comorbidities, such as depressive disorders and other anxiety disorders, as well as having an elevated lifetime risk of suicide (Strawn et al., 2018).

The therapeutic approach to GAD is multifaceted, involving a combination of psychotherapy and pharmacotherapy aimed at reducing symptoms and improving patients' quality of life. Studies have shown that psychotherapy, particularly cognitive-behavioral therapy (CBT), when combined with medication, enhances therapeutic effects, improves treatment adherence, and minimizes adverse effects related to pharmacotherapy (Strawn et al., 2018). Among the most studied pharmacological treatments are selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), as well as other agents such as benzodiazepines and atypical antipsychotics, with quetiapine being particularly notable (Baldacara et al., 2024).

Despite the wide range of therapeutic options, treating GAD still presents clinical challenges, particularly in selecting the most appropriate regimen for each patient. Combination therapies have shown positive results, but effective treatment depends on continuous symptom assessment, patient response to medications, and the suitability of the psychotherapy offered. In Brazil, the efficacy of psychopharmacological and psychotherapeutic interventions has been widely studied, but the literature still lacks more in-depth investigations comparing different treatments and determining the ideal duration of therapy to ensure better long-term outcomes (Baldacara et al., 2024).

This article aims to review the most effective therapeutic approaches for treating GAD, focusing on pharmacological and psychotherapeutic alternatives and discussing the clinical challenges encountered in medical practice. Through a critical analysis of available evidence, the goal is to contribute to updating knowledge on best practices for managing this prevalent and debilitating condition.

METHODOLOGY

This systematic literature review aims to synthesize the most recent evidence on the treatment of Generalized Anxiety Disorder (GAD). Articles were searched in the PubMed database using the descriptors "Generalized Anxiety Disorder" and "Treatment," with a publication limit of the last five years, covering studies published between 2013 and 2023. Inclusion criteria were strictly defined, selecting only articles directly addressing GAD treatment, focusing on pharmacological or psychotherapeutic therapies, including original studies such as randomized clinical trials, systematic reviews, and meta-analyses.

Exclusion criteria were based on specific factors: studies not addressing GAD treatment, those not available on PubMed, or those lacking relevant data on therapeutic interventions were discarded. Additionally, articles that did not allow for a critical evaluation of treatment efficacy, such as case reports or opinion studies, were excluded. Study selection was conducted by two independent reviewers who evaluated titles, abstracts, and full texts of the identified articles.

The analysis of selected articles focused on the types of treatments evaluated, their therapeutic effects, and observed clinical outcomes. The methodological quality of the studies was assessed according to guidelines for critical evaluation of clinical studies. All search, selection, and analysis processes were documented transparently to ensure reproducibility and review quality.

RESULTS AND DISCUSSION

The treatment of Generalized Anxiety Disorder (GAD) remains a significant clinical challenge, particularly in selecting the most effective therapeutic approaches and considering the specificities of the disorder. GAD, characterized by excessive and persistent worries about various everyday issues, affects a large portion of the global population, and treatments must be carefully selected for each patient, taking into account symptom severity, comorbidities, and individual preferences.

Therapeutic guidelines recommend both medication and psychotherapy, with the combination of both proving effective, especially in cases of moderate to severe GAD. Psychotherapy, particularly Cognitive-Behavioral Therapy (CBT), has emerged as a first-line treatment, effective in modifying dysfunctional thought patterns and reducing anxiety. Additionally, mindfulness-based approaches, such as Mindfulness-Based Stress Reduction (MBSR), have shown efficacy, with benefits comparable to traditional CBT (Locke, Kirst, &

Shultz, 2015). However, the combination of psychotherapy and medication may be particularly beneficial, potentially reducing relapse rates even after two years of follow-up.

Regarding medications, selective serotonin reuptake inhibitors (SSRIs) are widely recognized as a first-line treatment for GAD. Studies have demonstrated the efficacy of these antidepressants in modulating serotonin levels and reducing anxiety symptoms (Strawn et al., 2018). Venlafaxine, a serotonin-norepinephrine reuptake inhibitor (SNRI), has also proven effective for GAD treatment and is well-tolerated by patients, although blood pressure monitoring is necessary, especially at higher doses (Strawn et al., 2018). On the other hand, bupropion, while effective in treating comorbidities such as depression, is not indicated for GAD due to the risk of anxiogenic effects in some patients (Locke, Kirst, & Shultz, 2015).

However, the use of benzodiazepines, while effective for immediate relief of anxiety symptoms, presents significant clinical challenges. Dependence, abuse risk, and long-term adverse effects are limiting factors in their use, which is why NICE guidelines recommend their use only in short-term situations during crises (Locke, Kirst, & Shultz, 2015). Available evidence suggests that benzodiazepines, while effective for immediate treatment, do not contribute to long-term improvement compared to other treatment options such as SSRIs and CBT (Strawn et al., 2018).

In addition to pharmacological and psychotherapeutic treatments, the use of second-line therapies, such as pregabalin and quetiapine, has been studied with mixed results. Pregabalin has proven more effective than a placebo but is inferior to lorazepam in controlling anxiety (Locke, Kirst, & Shultz, 2015). Quetiapine, while effective for GAD, has a significant side effect profile, including weight gain and increased risk of diabetes mellitus, limiting its use to patients who have not responded to other therapeutic options (Strawn et al., 2018).

In the reviewed clinical studies, it was observed that the combination of psychotherapy and medication offers the best results for GAD treatment. The evidence that CBT and mindfulness-based approaches can significantly reduce anxiety symptoms is robust, with studies showing that these therapies have effects similar to or superior to other conventional psychotherapeutic treatments. Specifically, CBT stands out for its ability to modify thought and behavior patterns associated with GAD, making it the first choice in non-pharmacological therapies (Locke, Kirst, & Shultz, 2015).

Regarding medications, SSRIs remain the most recommended first-line pharmacological therapy. Studies have shown that these medications have a slower onset of action but, once titrated to the appropriate dose, are effective in reducing GAD symptoms. Additionally, the side effects of SSRIs tend to be more tolerable than other classes of medications, such as tricyclic antidepressants (TCAs), which, while effective, have a more severe side effect profile (Strawn et al., 2018). Venlafaxine, despite a moderate risk of increased blood pressure, has proven effective for GAD, with additional benefits observed in patients with comorbidities such as depression and panic disorders (Strawn et al., 2018).

On the other hand, the use of benzodiazepines has been highly limited due to the high risk of dependence and other adverse effects. While these medications are effective in rapidly reducing anxiety symptoms, they do not offer long-term benefits, restricting their use to emergency and short-term interventions, as recommended by guidelines (Locke, Kirst, & Shultz, 2015).

Finally, second-line therapies, such as pregabalin and quetiapine, have shown mixed results, being more effective in some cases but with substantial side effects that hinder their widespread use. Pregabalin has proven useful but not as effective as other first-line treatments, such as benzodiazepines, for anxiety control (Locke, Kirst, & Shultz, 2015). Quetiapine, despite its efficacy, carries a significant risk of weight gain and metabolic complications, limiting its application to treatment-resistant GAD cases (Strawn et al., 2018).

These results reinforce the importance of individualized treatment for GAD, considering patient preferences, symptom severity, and associated comorbidities. The combination of psychotherapy, particularly CBT, and medication appears to be the most effective strategy, but continuous monitoring and treatment adaptation are essential to ensure lasting results.

CONCLUSION

The treatment of Generalized Anxiety Disorder (GAD) requires a multimodal and individualized approach, given the complexity and variability of symptoms presented by patients. The combination of pharmacological and psychotherapeutic therapies remains the most effective strategy, with Cognitive-Behavioral Therapy (CBT) standing out as a first-line intervention, primarily due to its ability to modify dysfunctional thought patterns and

promote anxiety coping. Additionally, mindfulness-based approaches have also shown positive results, with efficacy comparable to CBT.

In the pharmacological field, selective serotonin reuptake inhibitors (SSRIs) and venlafaxine are presented as first-line treatment options, widely recommended for their efficacy in reducing anxiety symptoms and their relatively favorable side effect profile. In contrast, the use of benzodiazepines, while effective for immediate symptom relief, presents significant challenges regarding dependence risk and long-term adverse effects, restricting their use to short-term treatments in emergencies.

Second-line therapies, such as pregabalin and quetiapine, have shown mixed results, with efficacy observed in some cases but significant side effects that limit their application. These treatments should be considered only when other more conventional options have not yielded satisfactory responses.

In conclusion, GAD treatment should be personalized, considering the individual characteristics of each patient, including symptom severity, comorbidities, and patient preferences for therapeutic approaches. The combination of psychotherapy, particularly CBT, with medications, primarily SSRIs and venlafaxine, offers the best chance for lasting symptom relief, but continuous monitoring and treatment adjustment are essential to ensure long-term efficacy.

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