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Benzodiazepine Dependence Presenting as Treatment-Resistant Anxiety in a 27-Year-Old Male with Generalized Anxiety Disorder: A Case Report from Pakistan

Qasim Zia[1#*], Amana Qayum[2#], Omer Ismail Khalid[3], Muhammad Zaki ud Din[4], Junaid Iqbal[5], Muhammad Sheeraz[6], Hafiz Raees Imtiaz Sindhu[7], Muhammad Nabeegh Khan[8], Muhammad Salman Khan[9]

[1]Ibne Seina Hospital & Research Institute, MMDC, Multan

[2]Sofia Medical University, Bulgaria

[3]Arrahma Hospital for Mental Health, Multan

[4]Ibne Seina Hospital & Research Institute, MMDC, Multan

[5]Ibne Seina Hospital & Research Institute, MMDC, Multan

[6]Nishtar Medical University, Multan

[7]Saeed Medicare Hospital, Mian Channu

[8]Nishtar Medical University, Multan

[9]Ibne Seina Hospital & Research Institute, MMDC, Multan

[#]First Authorship holders

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***Corresponding author:** Qasim Zia, Ibne Seina Hospital & Research Institute, MMDC, Multan

ABSTRACT

Background: Benzodiazepines are widely used for the acute management of anxiety due to rapid onset of action, but prolonged or unsupervised use carries substantial risk of tolerance, physiological dependence, and withdrawal. Rebound symptoms may closely mimic treatment-resistant anxiety, especially in patients with pre-existing generalized anxiety disorder (GAD). In regions with lax prescription oversight, such as Pakistan, benzodiazepine misuse is a growing clinical concern.

Case Presentation: We report a 27-year-old male with a previous diagnosis of GAD, medication-free for one year, who presented with dizziness, panic-like episodes, and anxiety. Initial treatment with alprazolam for two months resulted in dependence, evidenced by panic attacks and autonomic symptoms when doses were missed. He was subsequently trialed on paroxetine for three weeks, followed by venlafaxine, with adjunctive quetiapine at night and clonazepam. With this regimen and structured monitoring, the patient achieved stabilization.

Conclusion: This case illustrates how benzodiazepine dependence can masquerade as treatment-resistant anxiety in patients with GAD. Comprehensive assessment, recognition of withdrawal and rebound phenomena, careful pharmacological strategy, and incorporation of psychotherapy are essential for achieving clinical stability.

Keywords: Benzodiazepine dependence; Generalized anxiety disorder; Treatment-resistant anxiety; Venlafaxine; Clonazepam; Quetiapine; Pakistan

INTRODUCTION

Generalized anxiety disorder (GAD) is a prevalent psychiatric condition characterized by excessive, persistent worry, psychophysiological hyperarousal, and functional impairment.[1] Lifetime prevalence estimates range from 3% to 6% globally, with considerable underdiagnosis in South Asian populations.[2,3] The disorder is associated with sleep disturbances, autonomic symptoms, and impaired quality of life. Evidence-based treatment typically involves first-line pharmacotherapy with selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs), combined with structured psychotherapy such as cognitive behavioral therapy (CBT).[4,5]

Benzodiazepines are frequently prescribed for rapid symptom relief. However, their use is generally recommended only for short-term periods (2–4 weeks), as prolonged exposure leads to tolerance, dependence, and withdrawal.[6–8] Neurobiologically, benzodiazepine dependence results from adaptive changes at the γ-aminobutyric acid (GABA)_A receptor complex, including receptor downregulation and altered receptor sensitivity.[9,10] Clinically, dependence manifests as tolerance, withdrawal symptoms, and paradoxical hyperarousal when doses are missed, often mimicking treatment-resistant anxiety or relapse of underlying psychiatric illness.[6,8,11]

In Pakistan, benzodiazepines are easily available over the counter in some regions, and there is limited awareness among patients and some prescribers about the risks of dependence.[12–14] Misuse of benzodiazepines in outpatient populations has been reported as high as 20–30%, especially in young adults and patients with pre-existing anxiety disorders.[13,14] These factors make recognition of benzodiazepine-induced anxiety critical to prevent misdiagnosis and inappropriate polypharmacy.

This case report describes a 27-year-old male with a prior diagnosis of GAD who developed benzodiazepine dependence following short-term alprazolam use, leading to rebound panic-like symptoms. It highlights the challenges of differentiating benzodiazepine-induced symptoms from treatment-resistant anxiety and the importance of comprehensive, structured clinical management.

CASE PRESENTATION

Patient History and Presenting Complaint

The patient was a 27-year-old unmarried male with a history of GAD diagnosed during late adolescence. He had been medication-free for approximately one year prior to presentation. The patient reported the sudden onset of dizziness, palpitations, restlessness, and panic-like attacks, occurring multiple times per week. Symptoms were particularly triggered by stressful social or work-related situations. He described intense anticipatory anxiety before leaving home or attending crowded places and reported that dizziness worsened during episodes, accompanied by a sense of impending doom.

He had no history of depression, psychosis, or substance abuse. Family psychiatric history was non-contributory. Medical history was unremarkable, and there was no history of cardiovascular, neurological, or endocrine disorders.

Initial Management and Development of Dependence

The patient was initially prescribed alprazolam 0.5 mg twice daily for symptomatic relief of acute anxiety and dizziness. While the medication initially provided rapid improvement, within two months, he began experiencing panic-like attacks and dizziness when he missed a dose, consistent with early benzodiazepine dependence. He reported increased anxiety and somatic symptoms when attempting to skip doses, creating a cycle of psychological reliance.

Subsequent Pharmacological Interventions

Recognizing persistent anxiety and rebound symptoms, the patient was initiated on paroxetine, titrated to a standard therapeutic dose, for three weeks. Despite adequate adherence, his anxiety and autonomic symptoms persisted, likely due to ongoing benzodiazepine withdrawal phenomena that were insensitive to serotonergic modulation alone.

He was subsequently switched to venlafaxine extended-release, titrated to 225 mg daily, due to its dual serotonergic and noradrenergic mechanism, which addresses both psychic and somatic symptoms in GAD.[15,16] To manage residual insomnia and agitation, quetiapine 50 mg nightly was introduced. In addition, clonazepam 0.5 mg twice daily, a long-acting benzodiazepine, was added temporarily to prevent severe withdrawal during the transition period.[17,18]

Mental Status Examination and Investigations

On examination, he appeared anxious with mild psychomotor agitation. Speech was coherent, thought processes were logical, and insight was partial. There were no perceptual disturbances, delusions, or suicidal ideation. Physical and neurological examinations were unremarkable. Laboratory investigations, including complete blood count, renal and liver function tests, thyroid profile, and electrolytes, were within normal limits.

Diagnostic Formulation

The patient met criteria for benzodiazepine dependence, manifesting as rebound anxiety and panic-like episodes, in the context of underlying GAD. The temporal relationship between alprazolam use and symptom escalation upon missed doses supported this diagnosis, differentiating it from primary treatment-resistant anxiety.

MANAGEMENT PLAN

Pharmacological Strategy

The management focused on stabilizing symptoms and discontinuing benzodiazepines safely. Clonazepam was maintained temporarily, given its long half-life, facilitating smoother tapering and reduced withdrawal severity. A structured tapering plan over 8–10 weeks was implemented, with close monitoring for autonomic or psychological withdrawal symptoms.[17,18]

Venlafaxine therapy was continued at an optimized dose, given evidence of efficacy in GAD and coexisting somatic symptoms.[15,16,19] Quetiapine was continued as adjunctive therapy for insomnia, with plans for dose reduction after stabilization.

Non-Pharmacological Interventions

The patient underwent cognitive behavioral therapy (CBT) targeting panic symptom control, coping strategies for anticipatory anxiety, and techniques for managing rebound symptoms during benzodiazepine tapering. Psychoeducation focused on the neurobiological basis of dependence, the mechanism of withdrawal symptoms, and strategies to prevent relapse.[20,21] Weekly follow-up ensured adherence, symptom monitoring, and psychological support.

Outcome and Follow-Up

The patient tolerated gradual discontinuation of clonazepam without significant withdrawal. Over three months, anxiety severity, panic episodes, and dizziness resolved. Sleep quality improved, and occupational and social functioning returned to baseline. At six-month follow-up, he remained on venlafaxine and quetiapine, free from benzodiazepines, with sustained clinical and functional recovery.

DISCUSSION

This case underscores the clinical complexity of benzodiazepine dependence masquerading as treatment-resistant anxiety, especially in patients with underlying GAD. Even short-term benzodiazepine use (two months in this case) can induce tolerance and dependence.[6,18] Clinicians must differentiate between rebound symptoms due to dependence and genuine treatment-resistant anxiety to avoid unnecessary polypharmacy.

Pathophysiology and Pharmacology

Benzodiazepine dependence results from down regulation of GABA_A receptors and decreased receptor sensitivity, leading to tolerance and heightened physiological arousal upon dose reduction.[9,10] Alprazolam, with a short half-life and high potency, is particularly prone to inducing withdrawal phenomena, including dizziness, palpitations, and panic-like episodes.[18,19] Transitioning to a long-acting benzodiazepine, clonazepam, allows stabilization and mitigates abrupt withdrawal effects.[17]

Venlafaxine's dual serotonergic and noradrenergic action addresses both psychic and somatic symptoms, offering superior control of rebound anxiety compared to SSRIs in some cases.[15,16] Quetiapine, used adjunctively for sleep, targets hyperarousal and facilitates overall stabilization.[21]

Regional and Public Health Considerations

In Pakistan, benzodiazepine misuse is facilitated by over-the-counter availability, limited regulatory enforcement, and low awareness of dependence risks.[12–14,22] Early recognition, structured tapering, and integration of psychotherapy are essential to reduce morbidity and prevent chronic misuse. This case illustrates the importance of detailed medication history, patient education, and clinician vigilance in managing

benzodiazepine-related complications.

Clinical Implications

- Benzodiazepine dependence should be considered in patients presenting with apparent treatment-resistant anxiety.
- Short-acting benzodiazepines are particularly high-risk for rapid dependence.
- Structured tapering using long-acting benzodiazepines and non-pharmacological interventions improves outcomes.
- Venlafaxine may offer advantages over SSRIs for somatic symptoms and rebound anxiety in GAD patients.

CONCLUSION

Benzodiazepine dependence can present as treatment-resistant anxiety, particularly in patients with underlying GAD. Comprehensive assessment, recognition of withdrawal and rebound phenomena, structured tapering, continued evidence-based pharmacotherapy, and incorporation of psychotherapy is critical for achieving sustained recovery.

Patient Consent

Written informed consent was obtained. Identifying information was anonymized.

Conflicts of Interest

None declared.

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