Suicide Risk Among Patients with Bipolar Disorder: The Role of Sleep Disruption Versus Benzodiazepine Use

To the Editor: We read with great interest the recent report by Saulnier and colleagues[1] examining suicide mortality among Veterans Health Administration (VHA) patients diagnosed with bipolar disorder. The authors' focus on identifying predictors of suicide risk in this vulnerable population is both commendable and much needed. Their central finding—that benzodiazepine use is associated with increased suicide risk—adds to a growing yet divided literature on this topic, in which epidemiological studies show elevated risk for suicide with benzodiazepine use[1–4] while longitudinal/interventional studies demonstrate reduced risk.[5–7] We would like to offer several considerations to aid in interpreting the present study.

The study reports that VHA patients with bipolar disorder who received benzodiazepine prescriptions for 30 days or more had a significantly elevated risk of suicide (hazard ratio = 1.58). However, it remains unclear whether benzodiazepine use occurred at the time of death or simply at some point within the year preceding the index diagnosis of bipolar disorder. This temporal ambiguity limits causal inference.

Moreover, the medication groupings used in the analysis pose interpretive challenges. For instance, the "sedative" category combines structurally dissimilar but functionally related agents (eg, zolpidem, eszopiclone, zaleplon) with off-label antidepressants used for sleep (eg, doxepin, trazodone) and melatonin receptor agonists (eg, melatonin, ramelteon), the latter of which are not sedating. Similarly, the study aggregates all benzodiazepines into a single category, despite notable differences in their clinical use. Clonazepam, diazepam, lorazepam, and alprazolam are often used for short- to medium-term anxiolysis, whereas agents like flurazepam, triazolam, and temazepam are specifically indicated for insomnia. Although the authors acknowledge the difficulty of distinguishing between a direct medication effect and an effect related to the underlying condition, analyzing medications by their pharmacological and clinical function could provide further clarity.[2]

The finding that only long-term benzodiazepine use was associated with increased suicide risk may indicate that the underlying condition requiring extended treatment—rather than the medication itself—is the primary driver of risk. For example, severe episodes of acute mania often necessitate sustained symptom management, and benzodiazepines are commonly prescribed during these periods to provide short-term relief. Similarly, individuals experiencing a suicidal crisis may receive a prolonged benzodiazepine prescription as part of crisis management, in which case any subsequent suicide attempt may reflect the severity of the crisis rather than a direct effect of the medication. Furthermore, benzodiazepines are known to induce pharmacologic tolerance; as their therapeutic effect diminishes over time, the original symptoms, such as anxiety or insomnia, may return or intensify, potentially exacerbating suicide risk.

This is particularly relevant in the case of sleep disturbance, a well-established risk factor for suicide[8–10] and a common challenge in individuals with bipolar disorder.[11] Multiple lines of evidence argue that disrupted sleep contributes directly to suicide risk through hopelessness, executive dysfunction, serotonergic dysfunction, hypothalamic-pituitary axis dysregulation, and nocturnal wakefulness.[12,13] Benzodiazepines are frequently prescribed when sleep disruptions persist despite mood-stabilizing treatments. Thus, prolonged benzodiazepine prescriptions may serve as a proxy for severe, treatment-resistant sleep disturbances rather than indicating an independent risk factor.

This alternative explanation, that benzodiazepine prescribing reflects severe sleep dysregulation, has critical clinical implications. If suicide risk is more closely tied to the underlying sleep disturbance than to the pharmacologic treatment, efforts to reduce suicide by limiting benzodiazepine use may overlook the more urgent need to identify and aggressively manage sleep problems in this population. Veterans with bipolar disorder who are prescribed any form of sleep aid—not just benzodiazepines—may benefit from enhanced suicide risk monitoring and comprehensive safety planning. Suicide prevention initiatives should explicitly recognize sleep disturbance as a high-risk state and ensure that affected individuals receive interventions targeting both sleep and suicidality.[14]

In summary, while the association between benzodiazepine use and suicide risk reported by Saulnier et al[1] is important, we urge caution in interpreting this relationship as causal without accounting for confounding by indication. Future research should strive to disentangle the effects of sleep disturbance from those of pharmacotherapy in shaping suicide risk. In the meantime, clinicians should integrate suicide safety planning into the care of all veterans with bipolar disorder who experience significant sleep disturbances, regardless of the specific sleep medication prescribed.

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