

## Lorazepam-Induced Delirium with Incoherent Speech in an Elderly Patient: A Case Report

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### ABSTRACT

Delirium is an acute confusional state associated with significant cognitive and functional impairment. Although all patients are at risk, elderly individuals and those with infections, pre-existing cognitive impairment, multiple comorbidities, or exposure to certain medications are particularly vulnerable. Incoherence refers to a disturbance in the logical organization of speech and thought, resulting in unintelligible communication. We report the case of a 74-year-old male with acute myeloid leukaemia and left ventricular failure who developed delirium and incoherent speech following the administration of lorazepam for sleep disturbances during hospitalization. Lorazepam, a benzodiazepine commonly prescribed for anxiety, insomnia, agitation, and seizures, acts via modulation of GABA-A receptors. Although generally considered safe, it may precipitate neuropsychiatric adverse effects such as delirium, particularly in elderly patients with multiple comorbidities.

This case highlights the importance of cautious benzodiazepine use in geriatric populations and underscores the need for vigilant pharmacovigilance reporting.

**Keywords:** Benzodiazepine, Lorazepam, Delirium, Incoherent speech, Adverse drug reaction

### 1. Introduction

The World Health Organization defines benzodiazepines as a class of sedative-hypnotic drugs used in the management of anxiety, insomnia, seizures, and alcohol withdrawal. These agents act as central nervous system depressants by functioning as positive allosteric modulators of the GABA-A receptor, thereby increasing the frequency of chloride channel opening and enhancing inhibitory neurotransmission<sup>1</sup>. Benzodiazepines

are indicated for a wide range of clinical conditions, including anxiety disorders, agitation, sleep disturbances, status epilepticus, and seizure disorders<sup>2</sup>. Commonly used agents such as lorazepam, clonazepam, and alprazolam are high-potency, short-acting benzodiazepines often prescribed alongside antipsychotics and mood stabilizers for the management of anxiety and sleep-related disorders<sup>3,4</sup>.

Incoherence refers to speech or thought processes that

are illogical, disorganized, and lack clear connections, rendering communication difficult to understand. It reflects a state of disturbed cognition and is often characterized by fragmented, rambling, or unintelligible speech. Incoherence is frequently associated with delirium, a neuropsychiatric syndrome characterized by disturbances in attention, awareness, perception, and cognition<sup>5</sup>. Data from VigiAccess indicate that approximately 43,179 adverse drug reactions have been reported with lorazepam use, of which 18% involve nervous system disorders and 19% involve psychiatric disorders<sup>6</sup>. Although lorazepam is widely regarded as effective and relatively safe, it may precipitate adverse neuropsychiatric effects, particularly in vulnerable populations. Drug-induced delirium is considered one of the most reversible causes of acute cognitive dysfunction<sup>7</sup>.

Delirium is thought to result from complex interactions involving oxidative stress, neurotransmitter imbalance, and disruptions in cerebral metabolism. Medications that interfere with neurotransmitter pathways-particularly those with anticholinergic properties, such as antipsychotics, antihistamines, and tricyclic antidepressants-are well-recognized contributors to delirium and associated cognitive disturbances<sup>8</sup>. There is a relative paucity of research in this area, likely due to overlapping treatment protocols and the multifactorial nature of delirium. This case highlights the need for cautious and monitored use of benzodiazepines in elderly patients and underscores the importance of reporting such adverse drug reactions to strengthen pharmacovigilance systems.

## 2. Case Presentation

This case was documented as part of a pharmacovigilance elective conducted by the Department of Pharmacology at Christian Medical College and Hospital, Ludhiana, which serves as an Adverse Drug Reaction (ADR) Monitoring Centre under the Pharmacovigilance Programme of India. The case was obtained from the Department of Haematology.

A 74-year-old male, a known case of acute myeloid leukaemia with monocytic differentiation, was admitted on 12 February 2026 for the second cycle of azacitidine and venetoclax therapy. At presentation, he reported fever, cough, and neck pain for two days. On general physical examination, his vital signs were stable except for fever. He was also a known case of left ventricular failure and was on ongoing treatment. Pedal oedema was noted around the ankles. Laboratory investigations were consistent with his underlying haematological condition, revealing anaemia and agranulocytosis. During hospitalization, the patient reported significant sleep disturbances, including difficulty initiating and maintaining sleep.

To address this, lorazepam 2 mg was prescribed orally at bedtime (HS) on 14 February 2026. Following initiation of therapy, the patient developed incoherent and irrelevant speech, altered sensorium, delirium, and episodes of urinary incontinence. On examination, he appeared confused, disoriented to time, place, and person, and intermittently unresponsive to verbal commands. There was no prior history of similar episodes. A differential diagnosis was considered, including drug-induced delirium secondary to lorazepam. Causality assessment using the Naranjo Adverse Drug Reaction Probability Scale yielded a score of 7, indicating a *probable* adverse drug reaction<sup>9</sup>.

Lorazepam was discontinued on 15 February 2026. Following withdrawal, the patient showed gradual clinical improvement. His sensorium improved, speech became coherent and relevant, delirium resolved, and urinary continence was regained. Complete resolution of symptoms was observed by 16 February 2026. The adverse drug reaction was reported to the pharmacovigilance database VigiFlow and recorded under IPC number IN-IPC-301229480.

A detailed description of causality, severity and preventability is shown in (Table 1).

**Table 1:** Detailed description of causality and severity of adverse drug reaction.

Causality, Severity and Preventability Assessment			
Assessment tool	Criteria	Result	Interpretation
Naranjo Adverse Drug Reaction Probability Scale <sup>9</sup>	Previous conclusive reports, Adverse event after drug, Improves on withdrawal, No alternative causes present, Objective evidence present.	Score 7	Probable adverse drug reaction
Modified Hartwig and Siegel Severity Assessment Scale <sup>10</sup>	The ADR required that treatment with the suspected drug be held, discontinued, No increase in hospitalisation.	Level 3	Moderate severity adverse drug reaction
Schumock and Thornton Preventability Scale <sup>11</sup>	Drug dose high for Geriatric patients, therapeutic drug monitoring required.	Yes	Probably preventable adverse drug reaction

## 3. Discussion

The World Health Organization defines an adverse drug reaction (ADR) as “a response which is noxious and unintended, and which occurs at doses normally used in humans for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological functions<sup>12</sup>.” Benzodiazepines are commonly prescribed for the management of insomnia due to their ability to increase total sleep duration and reduce sleep latency. Although non-pharmacological interventions and treatment of underlying causes are preferred, benzodiazepines continue to be widely used in clinical practice<sup>13</sup>. Lorazepam, in particular, is frequently utilized for sleep disturbances and agitation because of its intermediate duration of action and relatively predictable pharmacokinetics.

However, in the present case, lorazepam paradoxically precipitated neuropsychiatric manifestations, including incoherent speech, altered sensorium, and delirium<sup>14</sup>. This may be explained by its mechanism of action as a positive allosteric modulator of GABA-A receptors, leading to enhanced inhibitory neurotransmission<sup>15</sup>. In elderly patients, age-related pharmacokinetic and pharmacodynamic changes-including reduced hepatic metabolism, altered receptor sensitivity, and increased blood-brain barrier permeability-can amplify drug effects and predispose to central nervous system toxicity. Furthermore, benzodiazepines have been implicated as potential precipitating factors for delirium, particularly in hospitalized and geriatric populations. The underlying pathophysiology is multifactorial and involves neurotransmitter imbalance (notably

GABAergic excess and cholinergic deficiency), oxidative stress, and impaired cerebral metabolism<sup>4</sup>. These mechanisms contribute to acute cognitive dysfunction and behavioural disturbances.

In this case, multiple predisposing and precipitating factors likely contributed to the development of delirium. These include advanced age, underlying malignancy (acute myeloid leukaemia), comorbid cardiovascular disease (left ventricular failure), active infection, hospitalization, and exposure to benzodiazepine therapy. The presence of polypharmacy further increases susceptibility to adverse drug reactions. The patient was also receiving azacitidine and venetoclax as part of chemotherapy. Azacitidine acts as a hypomethylating agent, while venetoclax inhibits the BCL-2 protein, promoting apoptosis in malignant cells<sup>16</sup>. Although these agents are not directly associated with delirium, their systemic effects and contribution to overall physiological stress may have increased vulnerability to neuropsychiatric complications.

An important consideration in this case is the dosage of lorazepam. The patient received 2 mg at bedtime, which may be relatively high as an initial dose in a geriatric patient. Clinical guidelines generally recommend lower starting doses in elderly individuals due to increased sensitivity and reduced drug clearance. This supports the classification of the ADR as *probably preventable* based on the Schumock and Thornton criteria. The temporal relationship between drug administration and symptom onset, along with resolution following drug withdrawal (positive dechallenge), strongly supports a causal association. The Naranjo score of 7 further categorizes this reaction as *probable*. This case underscores the importance of cautious benzodiazepine prescribing in elderly patients, particularly in the presence of multiple risk factors. It also highlights the need for regular monitoring, dose individualization, and consideration of non-pharmacological alternatives for sleep disturbances in hospitalized patients.

#### 4. Limitations

This case report has certain limitations. First, as a single-patient observation, the findings cannot be generalized to a broader population. Second, although a strong temporal relationship and positive dechallenge support causality, rechallenge was not performed due to ethical considerations, limiting definitive confirmation. Third, the presence of multiple comorbidities and concurrent therapies may act as confounding factors in the development of delirium. Additionally, serum lorazepam levels were not measured, and objective neurocognitive assessment tools were not used, which could have strengthened the diagnostic evaluation.

#### 5. Future Directions

Further research is needed to better characterize the risk of benzodiazepine-induced delirium in elderly patients, particularly in the presence of multimorbidity and polypharmacy. Prospective studies evaluating safer dosing strategies and alternative therapies for insomnia in geriatric populations are warranted. There is also a need to strengthen pharmacovigilance systems through improved reporting and data integration to better identify rare or underreported adverse drug reactions. Incorporating geriatric prescribing guidelines, such as the Beers Criteria, into routine clinical practice may help reduce preventable adverse drug events.

Finally, greater emphasis should be placed on non-pharmacological interventions for sleep disturbances, including sleep hygiene, cognitive behavioral therapy, and environmental modifications, especially in hospitalized elderly patients.

#### 6. Conclusion

This case highlights that although benzodiazepines such as lorazepam are widely regarded as effective and relatively safe for the management of insomnia and anxiety, their use in elderly patients requires careful consideration. Age-related pharmacokinetic and pharmacodynamic changes, along with multiple comorbidities, increase susceptibility to adverse drug reactions, particularly neuropsychiatric manifestations such as delirium. The present case demonstrates a probable and preventable adverse drug reaction, supported by a clear temporal association and resolution upon drug withdrawal. It underscores the importance of individualized dosing, cautious prescribing, and close monitoring when using benzodiazepines in geriatric populations.

Furthermore, this report emphasizes the critical role of pharmacovigilance in identifying and documenting adverse drug reactions. Increased awareness and reporting can contribute to safer prescribing practices and improved patient outcomes.

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