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LETTER TO THE EDITOR

Successful initiation of catatonia treatment with oral diazepam in bipolar disorder: A case report

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Dear Editor,

Catatonia is a severe neuropsychiatric syndrome with life-threatening consequences (1). While lorazepam remains the first-line treatment (2), its limited availability in many countries, including ours, necessitates alternative approaches. Other benzodiazepines (such as diazepam, oxazepam, clonazepam, and midazolam) have been explored for catatonia treatment (3–6). Although intravenous diazepam has been studied in this context (6), to our knowledge, no prior reports have documented the successful initiation of catatonia treatment with oral diazepam. Here, we present two female patients with bipolar disorder who developed catatonia and were successfully treated with oral diazepam as the initial intervention. In both cases, catatonia was diagnosed according to DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition) criteria and monitored using the Bush-Francis Catatonia Rating Scale (BFCRS). Symptom remission occurred within 48 to 72 hours of initiating oral diazepam.

In the first case, a 61-year-old female with bipolar disorder presented with disorientation, disorganized speech and behavior, persecutory delusions, verbigeration, agitation, and reduced oral intake. Her symptoms had progressively worsened over 14 days prior to admission. One year earlier, she had experienced a catatonic episode that resolved with lorazepam initiation. Lorazepam had since been gradually tapered during outpatient follow-up. Upon admission, laboratory tests (blood/urine and cultures) and imaging studies (computed tomography (CT) and magnetic resonance imaging (MRI) to rule out delirium revealed no infectious or neurological abnormalities. The patient's initial BFCRS score was 10. Due to the unavailability of lorazepam in our country, oral diazepam (20 mg/day) was added to her treatment regimen, alongside her maintenance therapy with lamotrigine (300 mg/day). Her catatonic symptoms improved significantly within 24 hours, with the BFCRS score decreasing to 2 and reaching complete resolution (score of 0) within 48 hours. After remission for catatonic symptoms, clozapine was initiated to address mood symptoms. In the following days, the patient experienced mild sedation, which necessitated the gradual tapering of diazepam. She was discharged on day 19 of inpatient follow-up, having achieved remission of both catatonic and mood symptoms. At discharge, her medications included lamotrigine (300 mg/day) and clozapine (25 mg/day). During outpatient follow-up, the patient developed a depressive episode with psychotic features, including nihilistic delusions and catatonic symptoms such as stereotypy and verbigeration. Given her prior positive response to diazepam, 20 mg/day was initiated along with venlafaxine, in addition to her existing maintenance therapy. Her catatonic symptoms resolved first, followed by remission of depressive symptoms in the

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following days. Due to the recurrence of catatonic symptoms, diazepam (5 mg/day) was incorporated into her maintenance regimen. After three months, the patient developed pneumonia, requiring admission to the intensive care unit (ICU). During her ICU stay, all psychiatric medications were tapered and discontinued. Two weeks later, she presented to the emergency department with decreased motor activity and verbalization, reduced oral intake, stereotypic movement, and fixed gaze. Her initial BFCRS score was 17. Given the unavailability of lorazepam and her previous positive response to oral diazepam, diazepam (20 mg/day) was initiated after she was transferred to our inpatient clinic. The patient demonstrated a similar response to treatment, with gradual symptom resolution within 48 hours. Her BFCRS score decreased to 10 within the first 24 hours and returned to 0 by 48 hours. Alongside diazepam, treatment with clozapine, lamotrigine, and venlafaxine was reinstated as her catatonic symptoms resolved, and she was discharged on the fourth day of hospitalization.

The second case involved a 62-year-old female with a history of bipolar disorder who was admitted to the inpatient unit with a 10-day history of progressively worsening mutism, reduced oral intake, and psychomotor retardation. The patient's first psychiatric admission occurred at the age of 36 due to manic symptoms. Over the subsequent years, she required five inpatient admissions for manic episodes, one of which included psychotic features. Her most recent hospitalization had taken place eight months prior to the current admission, following another manic episode. She had been in remission on a regimen of clozapine 100 mg/day and lithium 600 mg/day. However, one month before this admission, she experienced lithium intoxication requiring emergency dialysis. Following this event, lithium was discontinued, and the patient was maintained on clozapine monotherapy. At admission, her BFCRS score was 16, indicating severe catatonia. In the absence of lorazepam, oral diazepam 5 mg was administered. Within one hour, the patient showed marked clinical improvement, with her BFCRS score reduced to 3. The diazepam dose was subsequently titrated to 20 mg/day, resulting in complete resolution of catatonic symptoms (BFCRS=0) within 72 hours. Following the resolution of catatonia, the patient exhibited depressive symptoms, for which lithium was cautiously reinitiated alongside ongoing clozapine and diazepam treatment. On day 18 of hospitalization, the patient developed acute respiratory failure secondary to aspiration pneumonia, necessitating ICU transfer. During her ICU stay, diazepam and clozapine were gradually tapered. After three days in the ICU, the patient was retransferred to the psychiatric unit, where clozapine and lithium were reintroduced. She remained clinically stable and was discharged on day 28 without residual catatonic or mood symptoms.

Although previous studies have documented the use of intravenous (IV) diazepam or oral diazepam for maintenance therapy (6–8), these cases suggest that oral diazepam can also be effective as a first-line acute treatment for catatonia, especially when lorazepam is unavailable. In earlier studies, clonazepam, oxazepam, and midazolam have also been considered in catatonia management (9). However, diazepam's rapid onset, long half-life, and active metabolites may provide both quick and sustained therapeutic effects, reducing the need for frequent dosing (10). Additionally, oral diazepam may be particularly beneficial for patients who cannot tolerate IV therapy or in settings where IV access is limited. Diazepam's longer half-life and faster peak plasma level compared to lorazepam may contribute to prolonged receptor activation, potentially sustaining therapeutic benefits while reducing withdrawal effects. Furthermore, the recurrence and resolution pattern observed in the first case underscores the importance of maintenance benzodiazepine therapy in recurrent catatonia.

To the best of our knowledge, this is the first report to document oral diazepam as an initial treatment for catatonia. While the small number of cases limits generalizability, the consistency, recurrence, and speed of response are clinically notable. These findings encourage clinicians to consider oral diazepam as an alternative treatment when lorazepam or IV administration is unavailable for managing catatonia. This case series was approved by the Ege University Ethics Committee (Approval No: 2024-4284). Written informed consent for publication was obtained from both patients.

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