mhc MENTAL HEALTH CLINICIAN

CASE REPORT Open Access

Loxapine for the treatment of psychosis in Lewy body dementia: A case report

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How to cite: Wu L, Jhawar A. Loxapine for the treatment of psychosis in Lewy body dementia: A case report. Ment Health Clin [Internet]. 2025;15(5):252-4. DOI: 10.9740/mhc.2025.10.252.

Submitted for Publication: April 23, 2025; **Accepted for Publication:** July 25, 2025

Abstract

Lewy body dementia (LBD) is a progressive neurological disorder characterized by dementia, parkinsonism, and psychotic symptoms. Treating psychosis in LBD is particularly challenging, especially given the high risk of extrapyramidal effects of antipsychotics commonly associated with this population. If treatment with an antipsychotic is warranted, low-potency antipsychotics are preferred; however, they may not be suitable for all patients because of adverse effect profiles, safety concerns, or logistical barriers. This case study illustrates how a patient diagnosed with LBD and unable to tolerate or access commonly used antipsychotics was effectively treated with low-dose loxapine.

Keywords: loxapine, case report, psychosis, Lewy body, dementia

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Disclosures: The authors have no conflicts of interest to disclose.

Introduction

A 2019 study noted that 15% of adults aged 68 years and older have dementia.[1] Treatment is initially aimed at slowing the cognitive decline; however, as the disease progresses, behavioral and psychosocial symptoms of dementia may present. These symptoms can include delusions, hallucinations, depression, anxiety, agitation, or disinhibition.[2]

Dementia with Lewy bodies is an umbrella term that includes Lewy body dementia (LBD) and Parkinson disease dementia (PDD). It accounts for 5% of all dementia diagnoses.[3] LBD is a progressive neurological disorder characterized by cognitive decline, parkinsonism, rapid eye movement (REM) sleep behavior, and psychotic symptoms, such as visual hallucinations and delusions.[2] LBD and PDD share overlapping treatment approaches, as they are neuropathologically indistinguishable except for the time to onset of dementia symptoms.[4] Although there is no cure, symptomatic treatment may be provided for hallucinations and delusions seen in LBD.

Treating psychosis in LBD is particularly challenging as this population is particularly susceptible to extrapyramidal adverse effects from antipsychotics. Neuroleptic sensitivity is seen in approximately 50% of patients and can result in fatal complications. It is theorized that dopamine and acetylcholine blockade are at least partly responsible for this phenomenon, which is a property of many antipsychotics, particularly those that are first-generation, which may explain why they are not recommended in LBD.[5] According to the Lewy Body Dementia Association, acetylcholinesterase inhibitors (AChEIs) are the first-line treatment of cognitive and psychiatric symptoms. Rivastigmine is the only AChEI that is FDA approved for treating LBD, but there is no comparative data among rivastigmine, donepezil, and galantamine to suggest that one is superior. If an AChEI is ineffective and the patient continues to have delusions or hallucinations not controlled by nonpharmacological interventions, antipsychotics may be considered. There is a US boxed warning for all antipsychotics noting an

increased all-cause mortality when used for the treatment of dementia related psychosis, so the risks versus benefits of treatment must be weighed very carefully.[6]

First-generation antipsychotics (FGAs) are generally not recommended in patients with LBD, as they can worsen parkinsonian symptoms and are more likely to cause neuroleptic sensitivity through their strong dopamine antagonism. Existing data suggest that second-generation antipsychotics (SGAs) may be cautiously used with close monitoring when needed because of the added serotonin 2A antagonism, which modulates dopamine in the nigrostriatal pathway.[5,7,8] Quetiapine and clozapine are the preferred agents because of the low dopamine-2 (D2) receptor antagonism to treat psychosis from LBD; however, their use may be limited due to lack of efficacy, tolerability concerns, or monitoring requirements. Despite the preference to use quetiapine in LBD, it is unclear if it is beneficial. A small study that enrolled 23 patients with LBD found that while quetiapine was well-tolerated and did not worsen parkinsonism, it did not demonstrate appreciable benefit in psychosis or agitation.[9] Clozapine has demonstrated benefit in multiple clinical trials for the treatment of psychosis in PDD, but its efficacy in LBD remains unestablished.[8] The need for frequent laboratory monitoring associated with clozapine may further limit its use. Although case reports suggest pimavanserin may be beneficial in LBD, high-quality evidence evaluating its safety and efficacy is lacking.[10-13] Additionally, its relatively high cost may limit broader use.

Given the limited availability of antipsychotic options, there is a clear need for alternatives to ensure that patients who do not respond to, cannot tolerate, or are not appropriate candidates for these agents still have access to safe and effective treatment. Although categorized as an FGA, loxapine could serve as a viable alternative given its distinctive pharmacokinetic and pharmacodynamic characteristics.[14,15] Of note, loxapine exhibits a high 5-HT2A to D2-binding ratio, similar to that of SGAs such as clozapine. Additionally, both loxapine and clozapine share a high affinity for D4 receptors, in contrast to other FGAs that predominantly target D2. To these authors' knowledge, there are no case reports or studies evaluating the use of loxapine for the treatment of psychosis in patients with LBD or PDD.

Case Report

An 80-year-old male diagnosed 5 years earlier with LBD and REM sleep disorder, presented to an outpatient clinic for ongoing LBD management. His past medical history is notable for hypertension, hyperlipidemia, chronic kidney disease, benign prostate hyperplasia, chronic pulmonary disease, glaucoma, and blindness.

The patient originally underwent neuropsychological evaluation for confusion, poor concentration, memory loss, vivid and recurrent visual hallucinations, hand tremors, and gait disturbances. Although Charles Bonnet Syndrome was initially considered, the presence of REM sleep disorder, cognitive decline, and motor symptoms made LBD the more likely diagnosis. The visual hallucinations—often of children and animals—occurred nightly; however, the patient denied all other psychiatric symptoms, including auditory hallucinations, dysphoria, paranoia, delusions, suicidal ideation, or homicidal ideation. Treatment was initiated with donepezil 5 mg, which led to a marked reduction, though not complete resolution, of hallucinations. The dose was increased to 10 mg nightly, resulting in complete remission of visual hallucinations within 6 months. For REM sleep behavior disorder, melatonin was titrated to 18 mg nightly, and trazodone 50 mg nightly was added. He remained stable on this regimen for approximately 4 years and maintained a fair level of independence in activities of daily living despite significant visual impairment.

After 4 years, the patient's wife reported a notable clinical decline characterized by worsening sleep, resurgence of visual hallucinations, and the onset of delusions—specifically, beliefs that strangers were entering their home in the evenings. These symptoms caused significant distress for both the patient and his wife, prompting consideration of antipsychotic treatment. A trial of quetiapine 12.5 mg nightly was initiated, resulting in some improvement in visual hallucinations. However, upon titration to 25 mg nightly in an attempt to achieve better symptom control, the patient developed increased confusion and more frequent hallucinations, now occurring throughout the day. As a result, the patient self-discontinued quetiapine. A brief trial of prazosin for sleep-related movements was also attempted but then discontinued due to symptom worsening. No additional psychomotor symptoms were documented in clinical notes.

Given the patient's blindness, cognitive impairment, and logistical challenges associated with frequent laboratory monitoring, clozapine was deemed an unfavorable option. Pimavanserin was ruled out because of high cost and nonformulary status. A multidisciplinary approach determined that loxapine 5 mg nightly could be tried. Despite limited data, the structural similarity to clozapine, which would be the next medication of choice, made this an appealing option. Three weeks after initiating loxapine, the patient presented to the emergency department for worsening REM sleep behavior disorder symptoms. At that time, trazodone was increased to 100 mg nightly. At a follow-up clinic visit approximately 1 month later, the patient reported significant improvement in symptoms. The frequency of visual hallucinations had decreased to once every 1 to 2 weeks, and he appeared markedly less distressed. He also denied experiencing any paranoia or delusions. There was one instance of a missed loxapine dose, which resulted in breakthrough hallucinations, further supporting its therapeutic effect.

The patient's positive response to loxapine 5 mg nightly was sustained at the 6-month follow-up without the need for dose

escalation. Both the patient and his wife felt that the medication was effective and well-tolerated, with no psychomotor adverse effects. Owing to the sedating properties of loxapine, trazodone was reduced to 75 mg nightly, while maintaining symptom control and improving quality of life. Both the patient and his wife expressed satisfaction with the current regimen.

Discussion

The management of neuropsychiatric symptoms in patients with LBD presents a significant clinical challenge because of their heightened sensitivity to antipsychotic medications and limited pharmacologic options. Quetiapine and clozapine are often considered the preferred antipsychotics due to their minimal D2 antagonism and lower risk of worsening Parkinson disease motor symptoms. However, in this specific case, the patient experienced worsened symptoms on quetiapine, and his comorbidities, coupled with logistical barriers to laboratory access, made adherence to clozapine monitoring requirements unrealistic.

First-generation antipsychotics are not recommended in LBD as the dopamine blockade can worsen symptoms and progress the illness. However, loxapine was selected as an alternative in this case based upon the structural and receptor binding similarities to clozapine and the theory that these similarities are unlikely to worsen the underlying disease.[15,16] In addition to these pharmacologic parallels, there are published reports of using loxapine in place of clozapine for treating schizophrenia symptoms, as it does not require frequent laboratory monitoring, making it a potentially preferable option.[15,16]

Conclusion

This case shows that loxapine may be a potential antipsychotic option for patients with LBD on an acetylcholinesterase inhibitor who are unable to tolerate or access clozapine, quetiapine, or pimavanserin. At the 6-month follow-up, the patient continued to experience a positive therapeutic effect from loxapine, with no reported adverse effects and the potential for sustained benefit over time. Additional studies would be valuable to better understand its safety and efficacy in this population.

References

1. Arvanitakis Z, Shah RC, Bennett DA. Diagnosis and management of dementia: review. JAMA. 2019;322(16):1589-99. DOI: 10.1001/jama.2019.4782
2. Cloak N, Schoo C, Al Khalili Y. Behavioral and psychological symptoms in dementia. In: *StatPearls*. StatPearls Publishing: 2025.
3. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US); [updated 2020 Jun 24]. Dementia with Lewy bodies; [updated 2021 Nov 24; viewed 2025 Apr 21]. Available from: https://medlineplus.gov/genetics/condition/dementia-with-lewy-bodies/.
4. Weintraub D, Hurtig HI. Presentation and management of psychosis in Parkinson's disease and dementia with Lewy bodies. Am J Psychiatry. 2007;164(10):1491-8. DOI: 10.1176/appi.ajp.2007.07040715
5. Baskys A. Lewy body dementia: the litmus test for neuroleptic sensitivity and extrapyramidal symptoms. J Clin Psychiatry. 2004;65 Suppl 11:16-22. PMID: 15264967
6. Naloxone hydrochloride injection, USP. Package insert. Hospira, Inc.; 2019.
7. McKeith IG, Dickson DW, Lowe J, Emre M, O'Brien JT, Feldman H, et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. Neurology. 2005;65(12):1863-72. Erratum in: Neurology. 2005;65(12):1992. DOI: 10.1212/01.wnl.0000187889.17253.b1
8. Divac N, Stojanović R, Savić Vujović K, Medić B, Damjanović A, Prostran M. The efficacy and safety of antipsychotic medications in the treatment of psychosis in patients with Parkinson's disease. Behav Neurol. 2016;2016:4938154. DOI: 10.1155/2016/4938154
9. Kurlan R, Cummings J, Raman R, Thal L, Alzheimer's Disease Cooperative Study Group. Quetiapine for agitation or psychosis in patients with dementia and parkinsonism. Neurology. 2007;68(17):1356-63. DOI: 10.1212/01.wnl.0000260060.60870.89
10. Abdul-Rahman T, Herrera-Calderón RE, Aderinto N, Kundu M, Wireko AA, Adebusoye FT, et al. Clearing the fog: a review of antipsychotics for parkinson's-related hallucinations: a focus on pimavanserin, quetiapine and clozapine. J Integr Neurosci. 2024;23(4):80. DOI: 10.31083/j.jin2304080
11. Rothenberg KG, McRae SG, Dominguez-Colman LM, Shutes-David A, Tsuang DW. Pimavanserin treatment for psychosis in patients with dementia with Lewy bodies: a case series. Am J Case Rep. 2023;24:e939806. DOI: 10.12659/AJCR.939806
12. Abadir A, Dalton R, Zheng W, Pincavitch J, Tripathi R. Neuroleptic sensitivity in dementia with Lewy body and use of pimavanserin in an inpatient setting: a case report. Am J Case Rep. 2022;23:e937397. DOI: 10.12659/AJCR.937397
13. Baker M, Song W, Fusick A. Pimavanserin use in Lewy body dementia: a case report demonstrating the medication's efficacy. Cureus. 2023;15(10):e46356. DOI: 10.7759/cureus.46356
14. Popovic D, Nuss P, Vieta E. Revisiting loxapine: a systematic review. Ann Gen Psychiatry. 2015;14:15. DOI: 10.1186/s12991-015-0053-3
15. Erley J, Goldsborough S, VandenBerg A, Audu A. Loxapine in patient with clozapine-resistant psychosis. Ment Health Clin. 2021;11(4):263-6. DOI: 10.9740/mhc.2021.07.263
16. Shrestha S, Agha RS, Khan Z, Shah K, Jain S. Considering loxapine instead of clozapine: a case series and literature review. Cureus. 2021;13(1):e12919. DOI: 10.7759/cureus.12919