

# Successful Use of High-Dose Brexpiprazole for Psychosis in Lewy Body Dementia without Adverse Effects

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## ABSTRACT

Low doses of brexpiprazole (0.5-2 mg per day) have been tried to treat dementia-related psychosis/agitation and Parkinson's disease psychosis. We report a 71-year-old patient with a diagnosis of probable dementia with Lewy body (DLB) whose psychotic symptoms benefit from a higher dose of brexpiprazole (4 mg per day) without adverse effects. Though more studies were needed to confirm the safety and efficacy of brexpiprazole in the treatment of DLB, this case suggests that brexpiprazole is a potential treatment choice and it is safe even at the maximum daily dose (i.e., 4 mg per day).

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## INTRODUCTION

The treatment of dementia with Lewy bodies (DLB) is complicated and difficult. The main symptoms of DLB are fluctuations of cognitive function, visual hallucinations, and parkinsonian symptoms.<sup>1</sup> Treating one of the main symptoms of DLB can make another one worse.<sup>2</sup> For example, antipsychotics in treating patients with DLB with psychosis could cause both irreversible parkinsonism and cognitive impairment. At present, treatment guidelines for DLB patients with visual hallucinations, if reducing dopaminergic regimens is impracticable, recommend starting treatment with an acetylcholinesterase inhibitor such as rivastigmine.<sup>3</sup> If the management is invalid, low doses of quetiapine or clozapine, both of which have lower incidence rate of drug-induced parkinsonism (DIP), could be considered if the treatment is strongly indicated.<sup>2</sup> Aripiprazole and brexpiprazole, partial dopamine D2 agonists, may confer a lower risk for DIP. Compared to aripiprazole, brexpiprazole is characterized by a more potent binding to serotonin 2A and 1A receptors, which may confer a lower propensity for DIP than aripiprazole.<sup>4</sup> We report a case of an elderly patient diagnosed with probable DLB. The patient's cognitive and motor symptoms responded to the prescription of rivastigmine and levodopa, and psychotic symptoms appeared to benefit from the treatment with brexpiprazole.

## CASE PRESENTATION

The patient of this case report was a 71-year-old Taiwanese woman whose disease initially manifested at age 69.

Symptoms manifestations were vivid visual hallucinations accompanied by the delusion of being possessed. According to the patient, she would often see demons when she was alone. She would put the blankets over her head because she was afraid the demons would come looking for her. She would sometimes run away in panic and hide in the room, as if the demons were chasing her. Also, she would act strangely and tell her family members that demons had taken over her body. Her husband and son were worried about the continued psychotic symptoms she was displaying. She was then admitted to the psychiatric acute ward for further assessment.

During hospitalization, in addition to the psychotic features, there was also dysthymia related to hallucinations, cognitive impairment, and rigidity of axial muscles with gait instability. We ordered a sequence of examinations. The results of hemogram and biochemistry tests (including complete blood count, glucose level, renal and liver functions), syphilis serologic tests, levels of vitamin B12 and folate, and thyroid function tests were all within normal limits. Magnetic resonance imaging of the brain showed an aging brain appearance with focal periventricular small vessel disease. The score of Mini-Mental State Examination was 18, with a cutoff score of 20/21, while her score on Clinical Dementia Rating scale was 1. A neuropsychological examination revealed the decline of executive dysfunction and the impairment of visuospatial skills, with reduced information retention abilities and decreased attention function. Single-photon emission computed tomography of the dopamine transporter (<sup>99m</sup>Tc-TRODAT-1) showed

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bilateral striatum dopaminergic neuronal function was decreased. No obvious abnormality was noted during the rapid eye movement period on polysomnography.

According to the findings mentioned above and her clinical symptoms, probable DLB was impressed. We started using brexpiprazole 2 mg/day in combination with the rivastigmine transdermal patch and levodopa. After a 2-week trial, there was no instability in gait, but limited improvement in psychotic symptoms was noted. Then we titrated brexpiprazole to 4 mg/day. After a 2-week trial, she described only minimal visual hallucination and a marked decrease in the feeling of being possessed. The cognitive function of the patient was reported to be at baseline over a 4-week period. After that, she was discharged and came to outpatient service regularly with treatment of brexpiprazole 4 mg, rivastigmine transdermal patch, and levodopa. Visual hallucination was mild and rare, which appeared maximum twice a month without obvious motor or cognitive symptoms for about a year.

We explained and discussed the treatment plan with the patient and family and then obtained a written informed consent from the patient.

## DISCUSSION

Recently, a meta-analysis reported the evidence for the pharmacotherapy options to treat different symptoms related to DLB.<sup>5</sup> For patients with DLB, donepezil may be effective for improving cognitive symptoms, and zonisamide may be effective for improving motor symptoms. Additionally, aripiprazole and yokukansan may improve neuropsychiatric symptoms. Among the clinical trials included in this meta-analysis, there were no trials evaluating the safety and efficacy of brexpiprazole in neuropsychiatric symptoms associated with DLB.

The reported case revealed that brexpiprazole improved the neuropsychiatric symptoms associated with DLB and the motor symptoms of DLB was not worsen under 4 mg brexpiprazole daily. The literature addressing the management of DLB with brexpiprazole is controversial and limited. Sanagawa et al<sup>6</sup> reported a patient with Parkinson's disease psychosis responding to 2 mg/day brexpiprazole augmentation without motor side effects, while Jackowiak and Chou<sup>7</sup> reported that a patient with Parkinson's disease and depression experienced a severe

worsening of parkinsonism associated with treatment with 1-2 mg/day of brexpiprazole.

These different results might be attributed to pharmacokinetic variations at different ages (i.e., the same dosage of brexpiprazole resulting in different brain concentrations of the medication) and DLB pathology-related striatal dopamine D2 receptors losses (different levels of variations in neurochemical receptors and neuronal loss in the course of the disease).<sup>5</sup> Additionally, the combined use of levodopa and brexpiprazole may influence both the tolerability and efficacy of brexpiprazole.<sup>5</sup> Due to the limited number of clinical studies of brexpiprazole on the neuropsychiatric symptoms of DLB, a well-conducted clinical trial is warranted to evaluate its clinical effectiveness in the future.

## CONCLUSION

We conclude that brexpiprazole augmentation might be considered in DLB patients with neuropsychiatric symptoms. Due to the warning, which from the U.S. Food and Drug Administration, of the higher mortality risk in elderly patients who have dementia when treating with antipsychotics, including brexpiprazole,<sup>8</sup> clinicians should have careful discussion of benefits and risks of using brexpiprazole in DLB with the patient and the caregivers.

**Informed Consent:** Informed consent was obtained from the patient who agreed to take part in the study.

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### MAIN POINTS

- The treatment of dementia with Lewy bodies (DLB) is complicated and difficult, treating one of the main symptoms of DLB can make another one worse.
- Partial dopamine D2 agonists, such as brexpiprazole, may confer a lower risk for drug-induced parkinsonism.
- The use of brexpiprazole in patients with DLB may improve the psychiatric symptoms without worsen motor symptoms.

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