Quetiapine for Psychosis in Parkinson's Disease Versus Dementia With Lewy Bodies

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Background: Most clinicians perceive psychosis in dementia with Lewy bodies (DLB) as more difficult to treat than Parkinson's disease, yet there are no reports comparing the antipsychotic response between the 2 disorders.

Method: All charts of Parkinson's disease and DLB patients at our Movement Disorders Center, Memorial Hospital of Rhode Island, Pawtucket, given quetiapine for psychosis were reviewed. Demographic data, including type and severity of psychosis, before and after Unified Parkinson's Disease Rating Scale (UPDRS)-motor scores, motor worsening, and treatment response (recorded as poor/none, partial, or total), were obtained. The chi-square test was used to assess differences in efficacy and tolerability of quetiapine between Parkinson's disease and DLB patients.

Results: Eighty-seven Parkinson's disease and 11 DLB patients with psychosis were analyzed. No significant difference in mean age, levodopa dose, quetiapine dose, duration of quetiapine use, or baseline UPDRS-motor score was noted between Parkinson's disease and DLB patients. Eighty percent (70/87) of Parkinson's disease patients and 90% (10/11) of DLB patients had partial to complete resolution of psychosis using quetiapine (p = .40). Motor worsening was noted at one point in 32% (28/87) of Parkinson's disease and 27% (3/11) of DLB patients over the duration of quetiapine use (p = .74).

Conclusion: Long-term quetiapine use was generally well tolerated in this geriatric Parkinson's disease and DLB population. Mild motor worsening occurred in some patients. No significant difference in long-term efficacy and motor worsening associated with quetiapine treatment was noted between the 2 disorders.

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Psychosis with delusions occurs in about 8% to 10% of the Parkinson's disease population[1–8] while up to 30% develop visual hallucinations.[1,9,10] Drug-induced psychosis is thought to be the single most important precipitant for nursing home placement in Parkinson's disease.[11,12] The emergence of atypical antipsychotic agents has allowed clinicians to control drug-induced psychosis without increasing parkinsonism for most, but not all, Parkinson's disease patients.

Demented Parkinson's disease patients have the highest risk of motor worsening in the setting of antipsychotic use.[13,14] Patients who have dementia with Lewy bodies (DLB) may be even more vulnerable due to their intrinsic neuroleptic sensitivity. Reports on risperidone[15] and olanzapine[16] use in DLB patients describe significant motor worsening. However, 2 separate reports on short-term quetiapine use in DLB patients are encouraging.[17,18] We are unaware of previous reports comparing long-term atypical antipsychotic response between Parkinson's disease and DLB.

METHOD

To compare the long-term effect of quetiapine for psychosis associated with Parkinson's disease versus DLB, a retrospective chart review of all geriatric patients diagnosed with Parkinson's disease and DLB at our Movement Disorders Center was performed. Demographic data, including the type and severity of psychosis, presence of dementia, dose and duration of quetiapine use, before and after Unified Parkinson's Disease Rating Scale (UPDRS)-

motor score,[19] and treatment response (recorded as poor/none, partial, total), were obtained.

A diagnosis of Parkinson's disease was given to patients with at least 3 of 4 cardinal features (resting tremor, rigidity, bradykinesia, and postural instability) and with a positive response to levodopa. All patients diagnosed with DLB satisfied the McKeith et al. criteria.[20] Dementia was defined according to the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV), criteria.[21] Response to quetiapine was recorded as poor, partial, or total based on the clinician's (J.H.F., H.H.F.) judgment.

A paired t test was used to compare the UPDRS-motor scores before and after quetiapine treatment. The chi-square test was used to assess differences in motor worsening and treatment response to quetiapine between Parkinson's disease and DLB.

RESULTS

Eighty-seven Parkinson's disease and 11 DLB patients with psychosis were retrospectively analyzed. All Parkinson's disease patients had drug-induced psychosis. Six of the 11 DLB patients had psychosis prior to levodopa treatment; the rest developed psychosis shortly after levodopa initiation. No significant difference in mean age (77 years vs. 77 years), levodopa dose (431 mg/day vs. 372 mg/day), quetiapine dose (58 mg/day vs. 69 mg/day), mean duration of quetiapine use (14 months vs. 14 months), or baseline UPDRS-motor score (45 vs. 40) was noted between Parkinson's disease and DLB patients. Dementia was noted in 56% (49/87) of Parkinson's disease patients after a minimum of 1 year from Parkinson's disease diagnosis. All DLB patients had dementia within 1 year of disease onset.

Poor or no response to quetiapine was noted in 20% (17/87) of Parkinson's disease and 9% (1/11) of DLB patients ($p = .40$). Eighty percent (70/87) of Parkinson's disease and 90% (10/11) of DLB patients had partial to complete resolution of psychosis using quetiapine. Motor worsening was noted at one point in 32% (28/87) of Parkinson's disease and 27% (3/11) of DLB patients over the duration of quetiapine use ($p = .74$). A significant increase from baseline to follow-up in mean UPDRS score (denoting worsening of condition) was seen among patients in both illness groups observed to have motor worsening (42 vs. 54; $p \leq .001$) compared with those who were not observed to have motor worsening (46 vs. 45; $p = .37$). Nonetheless, most worsening was noted to be mild, and no patient required hospitalization due to motor decline. Quetiapine treatment was discontinued in 18% (2/11) of DLB patients (none due to motor worsening) and 29% (25/87) of Parkinson's disease patients (10 due to increased parkinsonism). Seventy-two percent (71/98) of Parkinson's disease and DLB patients remained on quetiapine treatment for a mean duration of 14 months.

DISCUSSION

All previous open-label reports of quetiapine use for drug-induced psychosis in parkinsonian populations document its short-term efficacy and tolerability.[13,14,17,22–30] We echo this finding in our long-term study. Long-term, low-dose quetiapine use was generally well tolerated in this geriatric Parkinson's disease and DLB cohort. Over 70% remained on quetiapine treatment with continued efficacy. The use of quetiapine allowed us to introduce or increase levodopa doses as needed to alleviate parkinsonian symptoms, despite the history of psychosis, especially among our DLB patients.

Mild motor worsening occurred in some DLB and Parkinson's disease patients while receiving quetiapine. A statistically significant worsening between baseline and follow-up mean UPDRS-motor score was seen among Parkinson's disease and DLB patients observed to have motor decline. However, the motor worsening was not usually sufficient to warrant stopping quetiapine. Moreover, some of the increase in parkinsonism may have been due to disease progression, as many patients worsened over the course of a year or more.

No significant difference in long-term efficacy or motor worsening in association with quetiapine treatment was noted between the 2 disorders. These results suggest that, although DLB patients are neuroleptic sensitive, they appear to tolerate quetiapine as well as Parkinson's disease patients. Further analysis of these data is limited by the open-label, retrospective, and "naturalistic" nature of this study. Properly designed protocols are needed to confirm these observations.

Drug names: levodopa (Sinemet), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal).

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