Quetiapine as an Alternative to Clozapine in the Treatment of Dopamimetic Psychosis in Patients with Parkinson’s Disease

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There are many difficulties associated with the late stages of Parkinson’s disease (PD), but psychosis and agitation may be among the most disturbing for both patients and care givers, and often precipitate the pivotal decision for long-term nursing home placement. While the addition of antipsychotic drugs or the withdrawal of antiparkinsonian drugs may improve the behavioral problem, these strategies usually worsen the motor difficulties. Clozapine has been studied in PD for over a decade, and while it appears to be effective, there are safety and tolerability concerns associated with it. In addition, in New Jersey, Medicaid no longer pays for the home blood draws that are required for home-bound patients. This led to a situation in which we had patients who needed to stop clozapine and begin an alternative therapy. Because quetiapine seems particularly well suited to patients with PD based on in vitro and in vivo studies we have begun to try this medication in PD patients who need to stop clozapine. This article reports three case histories of patients with PD, confusion and dopamimetic psychosis who had been previously managed with clozapine and who were successfully switched to quetiapine. At doses from 12.5 to 150 mg/day quetiapine was well tolerated, resulting in behavioral improvement and no real increase in parkinsonism. These case histories raise the possibility that quetiapine may represent a viable alternative to clozapine in PD patients with dopamimetic psychosis and behavioral disturbances.

KEY WORDS: Parkinson’s disease; psychosis; quetiapine; clozapine; confusion.

INTRODUCTION

There are many difficulties associated with the late stages of Parkinson’s disease (PD), but psychosis and agitation may be among the most disturbing for both patients and care givers. Because antiparkinsonian medications have direct effects on CNS dopaminergic systems, it is not surprising that they often produce dramatic behavioral changes including hallucinations, delusions, agitation, and confusion. These behavioral changes may be more disturbing to patients and families than the motor changes, and often precipitate the pivotal decision for long-term nursing home placement (1). While the addition of antipsychotic drugs or the withdrawal of antiparkinsonian drugs may improve the behavioral problem, these strategies usually worsen the motor difficulties.

During the past 10 years, the atypical antipsychotics, which are associated with a lower risk of extrapyramidal side effects, have received particular attention as options for treating these problems. The prototypic atypical antipsychotic, clozapine, has been studied in Parkinson’s disease for over a decade. This drug is well suited for patients with PD because it has some selectivity for limbic and cortical region dopamine receptors (2,3). However, while demonstrating favorable results in approximately 90% of the more than 200 cases published, clozapine is associated with adverse effects including sedation, sci-
zures, hypotension, and agranulocytosis (4). Other adverse effects, including hypersalivation and a propensity to induce confusion and intellectual impairment, have also limited the use of clozapine in Parkinson's disease patients (3). It is the risk of agranulocytosis that mandates weekly or biweekly white blood cell counts and hence poses a great personal and financial burden to patients. This has become a particular problem because Medicare, in New Jersey, no longer pays for the home visits for blood draws that these patients require.

All of the other available atypical antipsychotics, including risperidone, olanzapine, and quetiapine are now being examined for patients with PD because they cause few extrapyramidal reactions and are not associated with a risk of agranulocytosis. There is considerable disagreement in the literature as to the efficacy and tolerability of risperidone in these patients (5-10). While some patients with PD can tolerate low doses of risperidone, our clinical experience is consistent with that of Rich et al. (5) and Ford et al. (6) in finding a high rate of increased rigidity in PD patients on risperidone. There are three published reports of case histories of olanzapine in PD patients and the drug is in a multisite controlled study. Two of these published studies suggest both efficacy and tolerability (11,12) and one does not (13).

Quetiapine, a novel dibenzothiazepine derivative, and the newest of the atypical antipsychotics, seems particularly well suited to patients with PD. PET studies indicate that, compared to typical antipsychotics, it has lower striatal D2 occupancy after administration of clinically relevant doses (14) and lower in vitro affinity for a1, histaminic and muscarinic receptors than clozapine and olanzapine (15). Furthermore, some evidence indicates that quetiapine may exhibit selectivity for limbic and cortical, over striatal, dopamine receptor blockade (15). Quetiapine is generally well tolerated, but, in contrast to clozapine, it is not associated with a risk of agranulocytosis. It therefore does not require weekly white blood cell counts and does not pose the inconvenience and financial burden of clozapine therapy.

Previous case reports have described the efficacy and tolerability of quetiapine in a small number of Parkinson's disease patients (16,17), raising the possibility that quetiapine may be an alternative to clozapine for late stage PD patients with psychotic symptoms. At our center we have many PD patients who are on clozapine but, because of the severity of the motor symptoms, are unable to go for weekly or biweekly CBCs. Recent changes in the regulations for New Jersey Medicare have eliminated home visits for blood draws, leaving a number of PD patients in a difficult position. This report details the first three cases in which we switched these patients from clozapine to quetiapine.

CASE REPORTS

Case 1

Mr. D, a 69-year-old man with a 20-year history of idiopathic Parkinson's disease, now Hoehn & Yahr (H-Y) stage III and treated with 1550 mg of levodopa (with carbidopa). There was no premorbid history of psychiatric illness but he has been treated with nortriptyline and alprazolam for depression for the past 5 years. He has a 2-year history of increasing confusion, with a mini-mental status exam (MMSE) of 17, as well as significant paranoid delusions and visual hallucinations.

He has been treated for the last 2 years with clozapine, 62.5 mg per day. There was some decrease in the paranoia and hallucinations, but the clozapine was stopped when Medicare would no longer pay for the home visits to have his CBC drawn.

Quetiapine was begun at 25 mg and gradually increased to 150 mg. There was a gradual improvement in the anxiety, agitation, paranoia and hallucinations. Now three months into therapy, his United Parkinson's Disease Rating Scale (UPDRS) has improved from 31.5 to 29.5 while maintaining the same levodopa dose. The MMSE is unchanged and his behavior is markedly improved.

Case 2

Mr. M is an 80-year-old man with a 6-year history of Diffuse Lewy body disease (PD/dementia with Lewy bodies or DLBD), now H-Y stage III and treated with 300 mg of levodopa (with carbidopa). There is no premorbid history of psychiatric illness but he does have a three year history of confusion, with a MMSE of 16, paranoid delusions and visual hallucinations. He initially tolerated clozapine but developed a decrease in platelet count and it was discontinued. He had also received a trial of olanzapine but became increasingly confused and it also was discontinued. He was begun on 12.5 mg of quetiapine with a subsequent increase to 25 mg. There was a dramatic difference in his paranoia, visual hallucina-