Management of Hallucinations and Psychosis in Parkinson's Disease

Marty L. Eng, PharmD; and Timothy E. Welty, MA, PharmD

Department of Pharmacy Practice, University of Kansas School of Pharmacy, Kansas City, Kansas

ABSTRACT

Background: Hallucinations and psychosis are common in patients with Parkinson's disease (PD), with reported prevalences of up to 48% and 80%, respectively. However, few randomized, double-blind, placebo-controlled trials evaluating the treatment options have appeared in the literature. The studies that have been published were complicated by lack of agreement on the diagnosis of psychosis in PD, poor completion rates, mixed populations that included dementia, and other issues. Several reviews, guidelines, and consensus statements have sought to establish standards for treating these symptoms of PD. In 2006, the American Academy of Neurology (AAN) published a practice guideline (based on articles published up to 2004) for management of depression, psychosis, and dementia in patients with PD. Since then, a number of relevant studies have been published.

Objective: The purpose of this article was to review data that have appeared in the literature since publication of the AAN guideline regarding the management of hallucinations and psychosis in PD.

Methods: A literature search of the PubMed, CINAHL, and PsychInfo databases was conducted for human studies published in English from January 2004 to June 2010. All clinical studies were included except case reports and case series. Studies with <20 participants were also excluded. Search terms included *psychosis, hallucinosis, hallucination, delusion, Parkinson, atypical antipsychotic, neuroleptic, aripiprazole, clozapine, olanzapine, quetiapine, risperidone,* and *ziprasidone*.

Results: Thirteen studies were included in the review: 3 studies of clozapine, 7 studies of quetiapine, 2 head-to-head trials comparing quetiapine and clozapine, and 1 noncomparative trial of clozapine or quetiapine interventions. Most of the studies included participants with a mean age in the early to mid 70s and a mean duration of PD typically >10 years.

Conclusions: Results of the identified studies suggested that patients with PD might benefit from long-term clozapine therapy. Results of the quetiapine studies were conflicting. However, no statistically significant difference in effectiveness was found between quetiapine and clozapine in comparative trials. The significance of the differences in treatment responses between patients with dementia and those without dementia remains unclear, and it was not possible to draw conclusions for or against other atypical antipsychotics because of insufficient evidence. Further studies are needed to address the methodologic issues in the current trials and to assess safety issues in larger cohorts. (*Am J Geriatr Pharmacother*. 2010;8:316–330) © 2010 Excerpta Medica Inc.

Key words: Parkinson's disease, hallucinosis, hallucinations, psychosis, atypical antipsychotics, neuroleptics.

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INTRODUCTION

Psychotic symptoms such as hallucinations and delusions are common in patients with Parkinson's disease (PD). The estimated prevalence of hallucinations ranges from ~10% to 48%, and the prevalence of delusions ranges from 3% to 80%.[1–9] Risk factors for the development of psychotic symptoms include cognitive impairment, dementia, age >65 years, advanced disease (>6 years' duration), advanced PD (Unified Parkinson Disease Rating Scale [UPDRS] score >44.5), presence of sleep disorders, concomitant depression, ocular dysfunction, family history of dementia, use of dopamine agonists, and axial parkinsonism.[10–13]

Recently, Ravina et al[14] developed diagnostic criteria for psychosis in PD. The characteristic symptoms include ≥1 of the following: illusions, false sense of presence, hallucinations, and delusions. The clinical definition of psychosis in PD also must include a primary diagnosis of PD using the UK Brain Bank Criteria, and the onset of symptoms must occur after the diagnosis of PD. In addition, psychotic symptoms must be recurrent or continuous for ≥1 month. These criteria rule out delirium and brief psychotic disorders. Associated features (eg, insight, dementia, PD treatment) may also be present and should be specified at the time of diagnosis. Other causes of psychotic symptoms that should be excluded are dementia with Lewy bodies (DLB), delirium, schizophrenia, schizoaffective disorder, delusional disorder, and mood disorder with psychotic features. Visual hallucinations tend to be more common but are often minor and less disruptive than delusions.[7,14] Both hallucinations and psychosis have been reported to persist throughout the course of PD.[15,16] These psychotic symptoms have been associated with increased caregiver burden, nursing home placement, and risk of death.[17–19]

Despite the high prevalence of hallucinations and delusions in PD, few randomized controlled trials (RCTs) have been published. Previous studies have typically been case studies, case series, retrospective and prospective observational studies, and open-label studies. The limitations inherent with such data create clinical uncertainties.

In 2006, Miyasaki et al[20] developed and published the American Academy of Neurology (AAN) practice guideline for the management of psychosis in PD in accordance with AAN standards for guideline development.[21] They concluded that clozapine should be considered for use based on one class I study and one class II study (comparison with quetiapine).[22,23] Based on a comparative trial of clozapine and quetiapine,[23] the recommendation was that quetiapine may be considered for use based on a lack of significant difference in effectiveness. Finally, it was recommended to avoid olanzapine because of a lack of response in treating psychotic symptoms and worsening of PD motor symptoms in 2 class II studies.[24,25]

The 2006 guideline included studies published before 2004. Because class I and II evidence was available, weaker, open-labeled studies and the plethora of case reports (class III or IV studies) were not included in the development of the guideline. Based on the guideline, clozapine or quetiapine may be used for hallucinations and psychosis. However, it is not clear which subgroups of patients would benefit from pharmacologic treatment or how long treatment should persist. For example, in Alzheimer's disease, behavioral and psychological symptoms of dementia (BPSD) appear to wax and wane in mild to moderate disease.[26,27] This allows for discontinuation of treatment or periodic dose reductions to minimize patient exposure to medications. However, in PD, BPSD have been reported to be persistent.[15,16]

The objective of this article was to review data that have appeared in the literature since publication of the AAN guideline regarding the management of hallucinations and psychosis in PD.

PATIENTS AND METHODS

The AAN guideline is based on studies published before 2004. Therefore, to review the subsequently published literature, a search of the PubMed, CINAHL, and PsychInfo databases was conducted for articles published between January 2004 and June 2010. The search was limited to English language and human studies. The following search terms were used: *psychosis, hallucinosis, hallucination, delusion, Parkinson, atypical antipsychotic, neuroleptic, aripiprazole, clozapine, olanzapine, quetiapine, risperidone,* and *ziprasidone*. All study designs were included except case reports, case series, and studies with <20 participants. References from published articles also were searched. Both authors reviewed the identified articles for inclusion in the review. Where disagreement about inclusion occurred, both authors met to review the criteria and resolve the difference of opinion. All published outcomes were included in the analysis of data.

The most commonly used scale in the reviewed studies was the Brief Psychiatric Rating Scale (BPRS).[28] Other scales included the Baylor Hallucination Questionnaire (BPDHQ; not validated), the Clinical Global Impression of Improvement (CGI) or Severity of Illness (CGI–SI),[29] the Hoehn and Yahr (H&Y),[30] the Mini-