Drug Therapies for Parkinson's Disease: A Database Analysis of Patient Compliance and Persistence

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ABSTRACT

Background: Evaluating medication adherence in Parkinson's disease (PD) is important to avoid erroneously attributing suboptimal patient outcomes from poor compliance to disease progression or adverse responses to medications.

Objective: This study of patients with PD who were new to PD drug therapy examined patient compliance and persistence, by drug, to provide a comprehensive investigation of medication-taking behavior in PD.

Methods: A retrospective analysis of patients receiving a new PD drug between March 1 and May 31, 2007, was conducted, using the IMS Health longitudinal prescription database, which contains ~50% of all retail prescriptions and >150 million patients in the United States. Patients were considered to have received a new PD drug if they initiated PD therapy for the first time, added adjunctive PD therapy, or switched one PD drug for another. Patients were categorized as naive to PD therapy (NT) or having prior PD therapy (PT), which included adjunctive use and switches. The PD medications evaluated were rasagiline, levodopa/carbidopa, levodopa/carbidopa/entacapone, the catechol-*O*-methyltransferase (COMT) inhibitors (entacapone and tolcapone), pramipexole, ropinirole, and selegiline. The study consisted of a 12-month look-back period (during which patients were required to be active in the database), a 3-month selection period (during which patients received their first prescription), and a 12-month observation period. Compliance was measured using the *medication possession ratio* (MPR; defined as the number of days' supply of medication divided by the number of available days of therapy, from first dispense date in the selection period to last dispense date in the observation period); *noncompliance* was defined as an MPR ≤80%. Persistence was measured as the duration (days) of uninterrupted therapy.

Results: A total of 29,682 patients with PD (19,673 NT, 10,009 PT) received a new PD drug and were analyzed. Of the 19,510 patients included in the compliance analysis, 10,438 (53.5%) had compliance rates >80% and 9072 (46.5%) were noncompliant. For all patients (NT and PT), compliance rates were significantly higher for patients taking rasagiline than for those taking other PD medications (all $P < 0.001$). For all patients, the highest mean number of persistent days of treatment (147.5) was reported for rasagiline, followed by levodopa/carbidopa/entacapone (146.9); persistence for both of these drugs was significantly higher than that for the comparator medications (rasagiline vs levodopa/carbidopa, $P = 0.002$; rasagiline vs pramipexole, $P = 0.003$; rasagiline vs COMT inhibitors, ropinirole, and selegiline, all $P < 0.001$; levodopa/carbidopa/entacapone vs levodopa/carbidopa, $P = 0.005$; levodopa/carbidopa/entacapone vs pramipexole, $P = 0.006$; levodopa/carbidopa/entacapone vs COMT inhibitors, ropinirole, and selegiline, all $P < 0.001$). Almost half of the patients (13,103; 44.1%) remained on their PD medication ≥90 days.

Conclusions: This study found a differential compliance and persistence across PD drug therapies. The compliance rate for rasagiline was significantly higher than that for all of the other PD medications. In addition, rasagiline and levodopa/carbidopa/entacapone were associated with significantly higher persistence rates than were the other PD medications. (*Am J Geriatr Pharmacother*. 2010;8:374–383) © 2010 Excerpta Medica Inc.

Key words: compliance, adherence, persistence, Parkinson's disease, antiparkinson medications, rasagiline.

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INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder that affects ~1 to 2 of every 1000 people in the United States.[1] The prevalence and incidence of PD increase exponentially in people >65 years of age, and it is estimated that 3% of this population are affected by the disease.[2] PD is second only to Alzheimer's disease as the most common neurodegenerative disorder in the United States.[1]

The symptoms of PD are caused by the destruction of dopaminergic neurons.[1,2] As more neurons die, symptoms progress, often leading to complete disability. In addition to disability, PD is associated with increased morbidity and total annual per-patient direct medical costs estimated at $23,101 versus $11,247 for those without PD.[1,3–5]

Drug treatment is the mainstay for the management of PD.[6] The goal of therapy in early PD is to increase dopaminergic activity in and around the basal ganglia.[7] This increased dopaminergic activity treats 3 of the cardinal symptoms of PD: rigidity, bradykinesia, and resting tremor.

Agents that are currently approved by the US Food and Drug Administration (FDA) for use in PD exert some of their effects via the following mechanisms: (1) dopamine replacement (levodopa); (2) stimulation of the postsynaptic dopamine D_2 receptors (ropinirole and pramipexole); (3) monoamine oxidase B inhibition (rasagiline and selegiline); and (4) inhibition of catechol-*O*-methyltransferase (COMT) (entacapone and tolcapone). Neither selegiline nor the COMT inhibitors are approved by the FDA for use as monotherapy for PD in the United States.

Management of PD requires that medications be taken as directed and for an indefinite period of time. Adherence to antiparkinson medication regimens is critical for controlling symptoms and maximizing the impact of these agents on patient outcomes.[8,9] Compliance (or adherence) can be defined as "the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen."[10] As in many chronic diseases,[11–14] drug nonadherence in PD appears to be common,[8,9,15–17] with one study[9] estimating PD adherence rates as low as 42% after 5 years. Therefore, evaluating medication adherence in PD is extremely important to avoid erroneously attributing suboptimal patient outcomes from poor compliance to disease progression or adverse responses to medications. Across a spectrum of disease states, poor adherence ultimately adds to the clinical and economic burdens of disease, negatively affecting patient outcomes.[18]

Although studies have previously evaluated compliance and its related impact on patient outcomes in PD,[9,15–17] only one study[15] has evaluated compliance across PD medications, and none have evaluated both compliance and persistence across PD medications. Persistence refers to the act of continuing treatment for the prescribed duration. Persistence can be defined as "the duration of time from initiation to discontinuation of therapy."[10] The objective of this study was to examine the compliance and persistence of patients new to PD drug therapy, by drug, to provide a comprehensive investigation of medication-taking behavior in PD.

PATIENTS AND METHODS

This retrospective analysis of patients with PD who were receiving a new therapy for specified PD symptoms over a 3-month period (March 1–May 31, 2007) was undertaken using longitudinal prescription information (LRx) extracted from the IMS LifeLink database (IMS Health, Inc., Plymouth Meeting, Pennsylvania). IMS Health is a provider of market intelligence to pharmaceutical and health care industries. The LRx database consists of anonymized prescription data from a sample of the IMS panel of retail pharmacies and pharmacy benefit managers. The database contains >150 million unique, anonymized patients and represents ~50% of retail prescriptions. The database includes prescriptions over a range of payment methods (cash, Medicaid, and third party).

The study consisted of a 12-month look-back period (during which patients were required to be active in the database), a 3-month selection period (during which patients received their first prescription), and a 12-month observation period.

To be considered new to PD drug therapy, patients must not have had any prescriptions filled for the index product in the 12 months before receiving their index prescription. Patients receiving a new PD drug included those initiating PD therapy for the first time, those adding adjunctive PD therapy, and those switching from one PD medication to another. Patients were categorized as naive to PD therapy (NT) or having prior PD therapy (PT), which included adjunctive use and switches. NT patients had not received a prescription for any PD product of interest during the 12 months before the index prescription. PT patients had received ≥1 prescription for a PD product of interest (other than the index product) during the 12 months before the index prescription.

All consecutive prescriptions filled for the same product were counted.