A REVIEW ON MEDICATION ADHERENCE IN PARKINSONISM PATIENTS

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ABSTRACT
Background: This literature review provides an overview of medication adherence issues in people with PD.
Methods: Articles were identified for this study using computerized database searches and journal hand searches. Computerized database searches of English-language articles. Results: We selected 10 articles measuring medication adherence in people with PD, which were published between 2000 and 2019 for assessment. All articles showed reduced medication adherence in Parkinsonism patients. Conclusion: Medication taking is a complex and multifaceted phenomena, patient-centered, theory-driven interventions are needed to improve medication adherence and quality of care and life in people with PD: Review indicate opportunities for professionals and lay people to work together to increase medication adherence in PD in hospital and community settings.

KEYWORDS: Medication adherence, Parkinsonism, Quality of life.

INTRODUCTION
Medication-related errors are common, but not often reported, in the treatment of Parkinson’s disease (PD), a chronic and disabling neurodegenerative disorder whose prevalence increases with age and is likely to rise with population ageing.[1] These errors can include the timing of medication ingestion for PD. Irregular timing, especially of L-Dopa and in later stages of the disease, can adversely affect those who have Parkinson disease well as their informal caregivers. Late, extra or missed doses can reduce medication efficacy—losing health gain, contributing to motor and nonmotor fluctuations and impairing function and quality of life.[2]

Timing errors for PD can take place in diverse health settings. The need for people with PD to receive the right medication at the right time in hospitals and care homes underpins the —Get it on timel campaign of Parkinson’s Societies internationally. Also common in community settings are the missed and mistimed doses attributable in whole or part to the actions of people with PD and their caregivers. This nonadherence has been reported to result mainly from being —too busy/forget or having—left home without drug. Approaches that health professionals use to identify and measure their timing errors can include error reports, record review, clinical surveillance, and observations of care.

However, people with PD, and their caregivers, can also observe formal and informal care, disclose their own timing mistakes and share their error-related concerns about professionals timing of medication for PD.[3] Formal safety assessments have tended to ignore lay errors and lay perspectives. Yet these perspectives link strongly to lay satisfaction with the health care experience. Also, they —often reveal how well a hospital system is operating and can stimulate important insights into the kinds of changes that are needed to close the chasm between the care provided and the care that should be provided. Health professionals need to be aware of, and responsive to, these perspectives if those who are most directly affected by PD are to trust them and engage in programs to identify, understand and manage timing errors.[8]

The muted voices of patients and caregivers have contributed to a paucity of research evidence on the nature and significance of the factors that can contribute in hospital and community settings to actual or perceived errors around medication timing for PD.

LITERATURE SEARCH METHODOLOGY
Articles were identified for this study using computerized database searches and journal hand searches. Computerized database searches of English-language articles were conducted in Cumulative Index of Allied Health Literature (2016-2018), Medline (2014-2018), PsycINFO (2014-2018), and PubMed (2002-2018). The following key words were used in these searches about medication adherence and associated
In general, medication adherence is evaluated as the percentage of prescribed doses taken during a defined period. The lowest adherence rate (33%) was from the findings of the study of 104 patients with PD who were aged 65 years and older and on Medicare Health Maintenance Organization in the Southern United States between 1996 and 2001 (Kulkarni et al., 2008).[6] The highest adherence rate (97.7%) was measured by electronic monitoring bottles, which recorded the date and time of cap opening in the prospective, observational study conducted in five European countries (Grosset et al., 2009).[11] Notably, medication adherence rates from retrospective, secondary analyses of medication insurance claims in the United States showed lower adherence rates compared with those of prospective, observation studies (ranges = 33%-72.7% and 60.4%-97.7%, respectively).

The observed discrepancy in adherence rates in this review may be because of differences in the methodology and participants for these studies. Measures of adherence varied among studies, including self-report using the MoriskyYGreen test, pill count, physician judgment, medication possession ratio based on pharmacy refill data, and electronic monitoring caps on all antiparkinsonian medications.[11] Timing nonadherence was the most frequently reported type in medication nonadherence in previous studies (Grosset et al., 2005; Leopold et al., 2004). With advanced PD, the medication regimen becomes complex, and people may take several doses during the day. Thus, timing nonadherence can result in either undertaking or overtaking medications. Correct timing clinician-centered approach (Gould & Mitty, 2010)[3] of doses is important to maintain the therapeutic level of antiparkinsonian medications in the blood stream. Irregular medication taking can result in motor fluctuation and dyskinesia because of intermittent dopamine intake and brief peaks of levodopa availability to the brain.[11] In contrast to suboptimal adherence, a group of people with PD experience overtaking or compulsive dopaminergic drug use, which is called dopamine dysregulation syndrome (DDS). People who have DDS were more likely to be younger at the onset of PD, be depressed, and drink more alcohol However, little known about the longitudinal clinical outcomes of DDS, so future studies are needed to explore the relationships.[7]

<table>
<thead>
<tr>
<th>Citation</th>
<th>Sample size</th>
<th>Study design and sampling</th>
<th>Measurement</th>
</tr>
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<tbody>
<tr>
<td>Yu-Jung Wei et al</td>
<td>7583</td>
<td>Retrospective secondary analysis, population-based</td>
<td>One-fourth of patients with PD had low adherence (MPR o 0.80, 28.7%) or had a short DOT (r400 days, 23.9%). Increasing adherence to APD therapy was associated with decreased healthcare utilization and expenditures.</td>
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<tr>
<td>Aline Aparecida Foppa et al</td>
<td>70</td>
<td>Quasi-experimental uncontrolled before- and after study carried out between September 2012 and March 2013 in a community pharmacy.</td>
<td>Seventy patients were followed up, showing a decrease in medicine-related problems (1.67 ± 1.34 to 0.8 ± 0.9 (p&lt;0.001), positive impact on adherence (from 37 to 10 non-adherent patients, p&lt;0.001).</td>
</tr>
<tr>
<td>David J Daley et al</td>
<td>80</td>
<td>A parallel, randomised controlled trial. Morisky Medication Adherence Scale-4</td>
<td>Positive impact on adherence</td>
</tr>
<tr>
<td>Stephen Buetow et al</td>
<td>20</td>
<td>Qualitative research</td>
<td>Five themes help to account for possible timing adherence errors by people with PD, their caregivers or professionals.</td>
</tr>
<tr>
<td>Davis, Edin, and Allen (2010)</td>
<td>3,119</td>
<td>Retrospective secondary analysis, population-based</td>
<td>Mean MPR = 0.58; adherence: 39%, nonadherence: 61%; at least one interruption of APD during 12 months: 32%; a large positive relationship between nonadherence and both medical and total healthcare costs (+$3,451, p &lt; 0.001, and +$2,383, p = .0053, respectively</td>
</tr>
<tr>
<td>Grosset et al. (2009)</td>
<td>112</td>
<td>Prospective, observational study</td>
<td>Total adherence: 97.7%; days adherence: 86.2%;</td>
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</table>
Factors of medication adherence in people with PD

Several associated factors of antiparkinsonian medication nonadherence were reported in previous studies. Factors of adherence to antiparkinsonian medications identified from the findings of previous studies were divided into six categories. Patient characteristics are age, gender, race, and risk-taking behaviours, and the social factor is lack of spouse/partner. Disease-related factors are cognition, mood disorder, and longer disease duration. Financial and health system barriers are low income and maintaining employment. Patient and provider relationship factors are regimen complexity/polypharmacy and poor knowledge of PD/education. Treatment-related factors are poor symptom control or quality of life.

Some factors in the framework could be modifiable; however, others may not be modifiable by the nature of the disease. For example, nonintentional nonadherence, or more simply, forgetting to take dosages, could be the area most amendable to interventions, which aim to improve medication adherence in people with PD. However, there are some gaps noted about the roles of patients’ beliefs, characteristics, and decision-making process in the area of adherence to antiparkinsonian medications. In addition, little is known about factors associated with nonadherence, including patients’ fear of higher dose medication, side effects, and limited options for future medication therapy. Thus far, the focus has been on the individual factors that influence medication adherence. However, it must be acknowledged that PD is a progressive disease.

In the early stages, many people with PD will be able to manage their medications independently; however, in the moderate to advanced stages, they may need additional help and support. Because most care for people with PD in the United States is provided at home by family members, family caregivers play vital roles in the care of moderate-to-advanced PD. Most people with PD (93%) at 10 years of the disease live at home, thus emphasizing the importance of the family caregiver. At home, family caregivers assist the individual with PD in safety, medication compliance, activities of daily living, and social involvement. As Schrag, Hovris, Morley, Quinn, and Jahanshahi (2006) noted, caregivers of people with PD experience a significant burden affecting physical, emotional, and social aspects of their quality of life. For instance, 90.4% of caregivers reported some level of caregiver strain in a multicenter, nationwide, observational longitudinal study. Notably, the domains of caregiver strain were shifted from social and time constraints in caregivers with the mild strain to physical and financial strains in those with moderate and severe strain. Therefore, management of PD including medication regimen does not equate to patient care alone but also necessitates education and support for their caregivers.

<table>
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<tr>
<th>Study</th>
<th>Patients</th>
<th>Design</th>
<th>Adherence Measures</th>
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<tr>
<td>Grosset et al. (2005)</td>
<td>54 patients</td>
<td>A single-center, observational study United Kingdom, for 3 months; U.K. Brain Bank criteria, taking at least one APM,</td>
<td>MEMS Adherence: 79.6% (43/54); suboptimal: 20.4% (11/54); timing compliance: poor; 11% for underusers, 25% for satisfactory users; poorer compliance associated with younger age, depression, more tablets per day</td>
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<tr>
<td>Kulkarni et al.</td>
<td>104 patients</td>
<td>Retrospective, longitudinal cohort, population-based</td>
<td>MPR ratings (0.42Y0.55); adherence: 33% suboptimal adherence: 67%; first year: 62.5%, second year: 64%, third year: 63.1%, fourth year: 72%, fifth year: 71.6%</td>
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<tr>
<td>Leopold et al.</td>
<td>39 patients with PD</td>
<td>One medical center Blind study</td>
<td>Adherence: 84.6%; suboptimal adherence: 15.3%; mistiming self-report: 73% (27/39); MEMS use: 82.1% (32/39)</td>
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<tr>
<td>Valldeoriola et al.</td>
<td>418 patients</td>
<td>Cross-sectional survey</td>
<td>Adherence rate; MoriskyYGreen test: 60.4%; physician’s opinion: 93.7%; positive correlates of adherence: high level of knowledge about PD, good clinical control, a spouse or life partner, higher incomes; negative correlates of adherence: cognitive impairment and psychiatric symptoms</td>
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INTREVENTION TO IMPROVE MEDICATION ADHERENCE

Because of its complexity and multifactorial nature, it is hard to find a single way to improve medication adherence. For instance, the authors of a recent Cochrane review concluded that current methods of improving adherence for chronic health problems are mostly complex and not very effective, so the full benefits of treatment cannot be realized.[7] Most medication adherence interventions for older adults focused on promoting knowledge and skills for medication taking; however, memory aids and self-monitoring strategies were underutilized. Involvement of family caregivers in medication adherence interventions for older adults was also suggested as one of the strategies to improve medication adherence.

In a study by Grosset and Grosset (2005)[4], active counselling groups were provided verbal and written information about the continuous dopaminergic theory and tailored written guidance on optimal medicine timing for their drug regimen. After the intervention, timing adherence, but not motor scores, was improved in the intervention group compared with the control group. In a phase II randomized controlled trial by Daley and colleagues (2014)[1], a cognitive-behavioural approach (i.e., adherence therapy) focused on modifying beliefs and exploring ambivalence toward medication was examined. The seven weekly one-to-one adherence therapy sessions showed improved self-reported adherence and quality of life. In addition, participants in the intervention group reported improvements in mobility, activities of daily living, emotional well-being, cognition, communication, and body discomfort.

In Germany, a standardized pharmaceutical care in community pharmacies showed improved health outcomes and quality of drug treatment compared with a comparison group. The standardized pharmaceutical care of 8 months was composed of assessment of drug-related problems, development of a pharmaceutical care plan, and evaluation of the patient’s health and drug regimen. Despite the advanced stage of PD, 35 of 50 participants were able to set up the reminder system without any help, and most participants in the study (91%) reported that short message service reminders worked well for them. As discussed above, a few intervention studies were conducted to improve medication adherence in people with PD, and they were delivered to people with PD in the community settings.

IMPLICATION AND SUGGESTION

Medication adherence has complex, multifactorial aspects as reported in previous studies. Accurate assessment of medication adherence is the first step to understanding medication-taking behaviors in people with PD using pill count, the MoriskyYGreen test, or medication diary or log. Home medication diary or log would be the easy and simple way to monitor the effectiveness and side effects of drug therapy.[7] In addition, using alarm clocks or smartphone applications as reminders would decrease unintended nonadherence such as forgetting to take a dose on time.

There is a need to understand each patient’s emotional readiness to initiate pharmacological therapy and expectations before initiating antiparkinsonian medications. Then, interventions aiming to improve medication adherence should be tailored to decrease or modify each patient’s identified barrier. Cognitive impairment and depression should also be assessed to evaluate the patient’s self-management skills. The need to include the caregiver in an intervention study should be evaluated. A partnership among various healthcare providers, patients with PD, and their caregivers using a patient-centered, nonjudgmental, and collaborative approach may improve medication adherence (Gould & Mitty, 2010).[5]

Medication costs may be one of the barriers associated with medication adherence in people with PD who are older adults with fixed incomes or who have left their work because of the symptoms of PD. Therefore, the information regarding medical insurance such as Medicare Part D should be provided at the early stage of the disease to plan their financial futures. Because of lack of experimental studies in the area, longitudinal, patient-centered, theory-driven randomized controlled trials in various settings are needed to provide strong evidence in the area. Utilizing advanced monitoring technologies and reminder systems may be beneficial for people with PD to improve medication adherence, clinical outcomes, and quality of life.

CONCLUSION

PD is a neurodegenerative disease that is more prevalent in older adults. Antiparkinsonian medications are the mainstay in symptom management of PD. However, medication nonadherence and suboptimal adherence have been documented in the previous studies. Because medication taking is a complex and multifacetted phenomena, patient-centered, theory-driven interventions are needed to improve medication adherence and quality of care and life in people with PD. Furthermore, the caregiver’s role in medication taking and adherence should be investigated in the future. Clinical pharmacist have a major role in counseling the patient and educating the bystanders about the disease and educate them to take medication correctly and there by improve the medication adherence.

REFERENCES

2. Ju Young Shin, Barbara Habermann et al, Medication Adherence in People With Parkinson Disease. DOI: 10.1097/JNN.0000000000000198