The Association Between Balance, Fear of Falling and Daily Activities in Drug Phases and Different Levels of Disease Severity in Patients with Parkinson's Disease

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• This study was approved at the Student Research Center of Iran University of Medical Sciences (Code of ethics: IR.IUMS.REC.1394.26664).

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Highlights

Knowledge about how drugs affect different functions in patient with Parkinson’s disease could lead to adopt specific strategy in drug on- and off-phases, resulting in enhanced function. Moreover, it is important to choose the best time (drug on- or off-phase) for the examination of changes in different functions, since drug phases may significantly affect different abilities and functions in these patients.

Plain Language Summary

Balance impairment and the subsequent increasing fear of falling are two main problems in Parkinson’s disease, which can affect the level of independence in daily activities. The chronic use of levodopa in these individuals results in motor fluctuation which disturbs various functions (balance, fear of falling, etc.). It is necessary for therapists to evaluate people with Parkinson's disease in several ways. First, the level of the disease severity and its impact on functional abilities should be examined. Then, therapists should be aware of drug responses. In this study, the effects of motor fluctuation in two drug phases (on- and off-phase) and severity of the disease on the relationship of balance and fear of falling and independence in activities of daily living were examined. The results showed significant relationships in both drug phases and different levels of disease's severity. Considering these associations can lead to better planning of the assessment timing and the therapeutic strategy in accordance with the drug phase and the severity of the disease.
The Association between Balance, Fear of Falling and Daily Activities in drug phases and different levels of disease severity in patients with Parkinson's disease

Abstract

Purpose: In the elderly, functional balance, fear of falling and independence in activities of daily living are interrelated; however, this association may change under the influence of drug phase and the severity of disease in individuals with idiopathic Parkinson's disease. The aim of this study was to investigate the relationship between functional balance, fear of falling and independence in activities of daily living in drug on- and off-phase.

Method: One hundred forty patients with Parkinson's Disease (mean age ± SD; 60.51± 12.32 years) were evaluated in terms of functional balance, fear of falling and independence in activities of daily living using the Berg Balance Scale, Fall Efficacy Scale-International, and Unified Parkinson Disease Rating Scale–activities of daily living, respectively, in drug on- and off -phases. Global disease rating was recorded by Hoehn and Yahr scale. Spearman coefficient, Kruskal-Wallis and Mann-Whitney tests were used to find out if the distribution of scale scores differs among levels of functional balance or among levels of disease severity.

Results: A strong correlation was found between the functional balance, fear of falling and independence in activities of daily living in both drug phases. The results also showed the significant difference in distribution of the Fall Efficacy Scale-International and Unified Parkinson Disease Rating Scale–activities of daily living scores among levels of functional balance (except independence in activities of daily living in drug off-phase). Also the distribution of the scores of Berg Balance Scale, Fall Efficacy Scale-International and Unified Parkinson Disease Rating Scale–activities of daily living showed significant differences among levels of disease severity.
Conclusion: The study showed a strong correlation between functional balance, fear of falling and independence in activities of daily living that can be affected by drug phase and severity of the disease. However, more studies are needed to understand this relationship.

Key words: Postural Balance, Fear, Activities of Daily Living, Fall, Parkinson's disease
Introduction

Parkinson's disease (PD) is a neurodegenerative disorder. One of its main symptoms is the inability to maintain posture and balance (Herman et al., 2014), a disturbance potentially related with falling and fear of falling (FOF) (Adkin et al., 2009). FOF is defined as a concern of falling during performing everyday life activities which may prevent an individual from carrying out these activities (Lindholm et al., 2014). According to previous studies in patients with PD, the decreased daily activities due to falling is considerable (estimated in about 44.1%) (Bloem et al., 2001). Avoiding daily activities due to FOF can increase dependence on others and social isolation while reducing the physical activity and quality of life (Deshpande et al., 2008; Kader et al., 2016; Rosqvist et al., 2017).

Levodopa is the primary treatment of PD and can be beneficial for almost all patients with PD. As the disease progresses, continuous use of the drug can lead to a series of motor complications (i.e. motor fluctuations). These people experience motor fluctuations between two drug phases called “on” (after taking the first dose of medication while symptoms of the disease are being controlled) and “off” (when symptoms re-emerge and the patient shows problems in motor function) (Ahlskog et al., 2001; Rodríguez-Molinero et al., 2017). Previous studies have examined the effects of motor fluctuations on various performances (such as balance, falling, etc.) in both drug phases of these patients. The best treatment response, medical interventions and rehabilitation programs must vary according to the patient's condition patient's motor performance and drug phase. Hence, understanding the relationship between factors such as fear of falling, functional balance abilities and independency in activities of daily living (ADL) could be useful for planning the most appropriate interventions for these patients (M. Morris et al., 1998; S. Morris et al., 2001). However, the relationship between these factors (i.e. functional balance, FOF and independence in ADL) has not yet been investigated with regard to the severity of the PD. On the other hand, most studies in this area
have been conducted in the drug on-phase. Meanwhile, functional balance, FOF and independence in ADL may significantly different in drug off-phase compared with on-phase (Foreman et al., 2011; Franchignoni et al., 2005).

Therefore, the purpose of this study was to investigate the relationship between functional balance, FOF and independence in ADL in people with idiopathic PD in drug on- and off-phase.

**Methods**

**Participants**

The study included 140 subjects with idiopathic PD (mean age [±SD] of 60.51 [±12.32], 66.42% males). The inclusion criteria were: 1. Diagnosis of idiopathic PD by a neurologist, based on UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria for PD (Hughes et al., 1992). 2. Have not evident cognitive impairment, (i.e. obtaining score of >21 on Mini Mental Status Examination (Godefroy et al., 2011)), and 3. Ability to understand test instructions in Persian language. All patients with a history of receiving rehabilitation services were excluded from the study.

This study was approved by the Ethics Committee of the Student Research Center at Iran University of Medical Sciences. Individuals signed informed consent before participating in this study.

**Procedure**

At the beginning of the study, patients were asked to not use levodopa when they came to the clinic. Assessments were first performed in the drug off-phase (i.e. 12 hours after last dose of levodopa and before first morning dose (S. Morris et al., 2001)) and later in the drug on-phase (i.e. 1 hour after taking the first dose of levodopa in the morning (S. Morris et al., 2001)).
Demographic information (age, sex, duration of disease, severity of disease based on Hoehn and Yahr, type of drugs, etc.), were obtained using the demographic questionnaire. Functional balance, FOF and independence in ADL were evaluated using Berg Balance Scale (BBS), Fall Efficacy Scale-International (FES-I) and Unified Parkinson Disease Rating Scale-ADL (UPDRS-ADL), respectively. The duration of evaluations varied 30-60 minutes (depending on duration of the drug's effect).

**Tools**

**Hoehn and Yahr (HY) Scale:** This scale was used to determine the level of PD progression. Based on this scale, severity of disease is divided into 5 levels (1-2-3-4-5). At the first level (1), condition is normal and at last level (5), patients are wheelchair bound (Goetz et al., 2004).

**Berg Balance Scale (BBS):** This scale is a basic test for evaluating functional balance and consists of 14 items; each of these items are scored from zero to four. The total BBS score is 0-56 and the higher score indicates better balance. BBS evaluates two basic dimensions of balance in everyday activities—Dynamic and Static. The instruments used include chronometer, ruler, chair, and a step. The Persian version of this scale has a high inter-rater reliability (ICC=0.99) and internal consistency (Cronbach's alpha=0.92) in patients with PD (Babaie-Ghazani et al., 2017).

**Fall Efficacy Scale-International (FES-I):** This is a 16-item scale that measures fear of falling. The total score of FES-I is between 0 and 64, with a higher score indicating more fear of falling. The Persian version of this scale has good test-retest reliability (Pearson correlation coefficient= 0.70) in the elderly population (Khajavi, 2013).
Unified Parkinson Disease Rating Scale–Activity of Daily Living (UPDRS–ADL): The second subset of the UPDRS scale (i.e. UPDRS-ADL) was used to measure individuals' ability and independence in ADL which contains 13 items (total score= 0-52). Higher scores on this scale indicates more dependency on others to carry out daily activities (Shulman et al., 2016).

**Statistical Method**

Normality of data was explored by the Kolmogorov-Smirnov test which indicates non-normal distribution of data. Spearman correlation coefficient was used to examine the relationship between functional balance (i.e. BBS score), FOF (i.e. FES-I score) and independence in ADL (i.e. UPDRS-ADL score). Spearman rank correlation coefficient values >0.60, 0.30-0.59 and >0.30 were considered as an indicative of strong, moderate and weak correlation, respectively (Xie et al., 2006).

Kruskal-Wallis H was investigated between the patients' FOF and UPDRS-ADL score among levels of functional balance. Levels of functional balance were divided into three groups using BBS score as follows: scores from 56 to 41, from 40 to 21, and less than 20 were considered as level 1, level 2 and level 3, respectively (Schneider et al., 2012).

Mann-Whitney test was used to examine differences between individuals' functional balance, FOF and independence in ADL among levels of PD severity. Different levels of PD severity were considered according to HY stages: stages 1 and 2 or mild were considered as level 1; and stages 3 and 4, or moderate/severe were considered as levels 2. Statistical analyses were performed separately for both drug phases (on and off).

**Results**

Ninety-four participants (67.14%) were in stage 1, 46 participants (32.85%) were in stage 2 based on HY. Mean score (± SD) of BBS in drug on-phase was 53.14 (±5.91), 44.25 (±13.90)
and in drug off-phase 51.67 (±7.76), 37.84 (±16.27) were at Stages 1 and 2 based on HY respectively.

A moderate correlation was found between functional balance and FOF in the drug on-phase \((r = -0.61, p <0.001)\) and the drug off-phase \((r = -0.70, p <0.001)\). Also, correlation between functional balance and independence in ADL was moderate in drug on-phase \((r = -0.52, p <0.001)\) and drug off-phase \((r = -0.62, p <0.001)\).

Based on results of Kruskal-Wallis H test, the distribution of the FES-I and UPDRS-ADL scores in drug on-phase \((H = 27.44\) and \(H = 12.80\), respectively) and drug off-phase \((H = 32.69\) and \(H = 21.09\), respectively) have significant differences among different levels of functional balance. Mean rank FES-I and UPDRS-ADL scores are shown in Table 1 for BBS levels of functional balance in the drug on- and off-phase. In all Kruskal-Wallis H tests, \(p\) values were <0.001.

The results of Man U Whitney indicated that the distribution of BBS, FES-I and UPDRS-ADL scores in drug on-and off-phase were significantly different among HY levels of PD severity. Mean rank scores of BBS, FES-I, and UPDRS-ADL in the drug on- and off-phase at different levels of PD severity are reported in Table 2, In all tests, \(p\) values were <0.001.

**Discussion**

The purpose of this study was to investigate the relationship between functional balance, FOF and independence in ADL in people with idiopathic PD in drug on- and off- phases. The results of this study showed that there was a significant difference between various levels of functional balance and severity of disease, FOF and independence in ADL in both drug on- and off-phases.

According to studies of Franchignoni et al. (2005), Bryant et al. (2015), and Landers et al. (2017), people with greater damage in balance show more FOF during their functions (Bryant
et al., 2015; Franchignoni et al., 2005; Landers et al., 2017). Also according to results of Landers et al. (2017) study, FOF is significantly different at different stages of severity of disease (Landers et al., 2017), which is aligned with results of our study. In addition, as suggested by Foreman et al. (2011) who used a correlation analysis, evaluation of FOF and independence in ADL at different levels of functional balance in drug off-phase gives more accurate information to therapists in these cases (Foreman et al., 2011). On the other hand, results at different levels of functional balance showed a significant change in independence in ADL in drug on- and off-phase. This outcome in our study may be due to a decrease in physical activity, which is due to a reduction in effect of dopamine medications in brain, which needs further investigation.

One of the important factors for independence in ADL, especially in those needing a standing position, is to maintain the balance and to control the posture. Landers et al (2017) found that patients with PD avoid doing such activities because of the lack of functional balance to prevent falling (Landers et al., 2017). The results of this study also showed that at higher (i.e. better) levels of functional balance, independence in ADL was higher. These results were more pronounced in drug off-phase which alters functional state of patients with PD.

Finally, findings of this study indicated that taking a plan of medicine (rehabilitation and medication) to improve balance of idiopathic in people with Parkinson's disease can help reduce FOF. It is noteworthy when individuals are less worried about falling during their ADL, their level of independence will be relatively higher.

Additionally, increasing dependence on others due to reduction of independence in ADL can increase the feeling of tiredness and burden among the caregivers. Since PD is a chronic and progressive disorder, interventions designed to improve the level of independence in ADL can indirectly help the caregivers (Bhatia et al., 2003).
Maintaining balance and posture in a standing position is essential for most of the daily activities of life (Dunsky et al., 2017). According to the results of this study, in people with more balance problem, the fear of falling and dependence on others was higher. This case was shown in this study with the progression of the disease as well as in the off-phase drug. We believe that consideration of balance training in rehabilitation program of these individuals can help maintain independence in everyday activities, even at advanced levels of disease and the off-phase drug (which symptoms of disease reappear). Of course, more comprehensive studies are needed to confirm this subject.

This study had some limitations. First, psychological factors were not considered in this study. Moreover, individuals were selected with convenience sampling method, and, thus, most of samples to were at stage 1 of PD severity. These limitations may reduce the degree of generalizability of the results. Hence, it is suggested that future studies consider these issues.

In conclusion, considering the relationship between functional balance, FOF and independence in ADL in patients with PD in drug on-off phases is critical to design an effective treatment plan. Identification and management of difficulties in balance and ADL as well as FOF, may increase the quality of life and the level of participation of individuals in social activities (regardless of severity of disease and drug phases).

**Ethical Considerations**

This study was approved at the Student Research Center of Iran University of Medical Sciences (Code Number: IR.IUMS.REC.1394.26664).

**Acknowledgment**

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Conflict of interest

The authors assert that there is no conflict of interest.

Table 1: Mean rank of FOF and ADL among BBS levels of Balance in people with idiopathic Parkinson’ disease (n=140)

<table>
<thead>
<tr>
<th>Level of BBS</th>
<th>FOF (FES-I)</th>
<th>ADL (UPDRS-ADL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>On drug phase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>52.59</td>
<td>58.63</td>
</tr>
<tr>
<td>2</td>
<td>94.13</td>
<td>88.35</td>
</tr>
<tr>
<td>3</td>
<td>111.50</td>
<td>100.08</td>
</tr>
<tr>
<td>Off drug phase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>51.50</td>
<td>55.72</td>
</tr>
<tr>
<td>2</td>
<td>82.14</td>
<td>80.56</td>
</tr>
<tr>
<td>3</td>
<td>99.00</td>
<td>76.42</td>
</tr>
</tbody>
</table>

BBS: Berg Balance Scale
FOF: Fear of Fall
FES-I: Fall Efficacy Scale-International
ADL: Activities of Daily Living
UPDRS-ADL: Unified Parkinson’s disease Rating Scale-Activities of Daily Living

Table 2: Mean rank of Balance, FOF and ADL among H-Y levels in people with idiopathic Parkinson’ disease (n=140)

<table>
<thead>
<tr>
<th>Level of H-Y</th>
<th>Balance (BBS)</th>
<th>FOF (FES-I)</th>
<th>ADL (UPDRS-ADL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>73.86</td>
<td>56.80</td>
<td>52.89</td>
</tr>
<tr>
<td>2</td>
<td>43.90</td>
<td>28.18</td>
<td>83.45</td>
</tr>
</tbody>
</table>

H-Y: Hoehn and Yahr
BBS: Berg Balance Scale
FOF: Fear of Fall
FES-I: Fall Efficacy Scale-International
ADL: Activities of Daily Living
UPDRS-ADL: Unified Parkinson’s disease Rating Scale-Activities of Daily Living
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