Falls in Parkinson’s disease. Causes and impact on patients’ quality of life

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Summary
The aim of this study was to investigate the prevalence of the different causes of falling in Parkinson’s disease (PD) and to evaluate the influence of falls on patients’ quality of life (QoL). We recruited 60 PD patients (31 with falls, 29 without falls). We found that falls were caused by: unstable posture (29.0%), freezing or festination (25.8%), sudden loss of postural reflexes (toppling falls) (25.8%), co-existing neurological disorders (6.5%), cardiological disorders (6.5%), and symptomatic orthostatic hypotension (3.2%). Duration of the disease was longer, its stage more advanced, daily levodopa dosage higher, and the proportion of patients with abnormalities in the EEG apparently greater in the group with falls. The presence of falls was found to be a factor contributing to a multidirectional negative impact on patients’ QoL. QoL also depended on impairment of cognitive function, daily dosage of levodopa, disease duration, disease progression, and sex. The results of this study underline the need to diagnose the causes of falls in order to institute appropriate treatment and to improve patients’ QoL.

KEY WORDS: falls, Parkinson’s disease, quality of life.

Introduction
Falls, which are a common symptom of advanced Parkinson’s disease (PD), may cause medical and psychological complications. Occurring in 50.8-68.3% of patients with PD (1-4), they have various causes and therefore require differential diagnosis. Falls in PD can be categorized as related to postural instability, freezing or festination, levodopa-induced dyskinesia, symptomatic orthostatic hypotension, sudden loss of postural reflexes (toppling falls), coexisting neurological or other medical disorders, and environmental factors (5,6). They may lead to injuries (including hip fracture), immobility, premature nursing home placement, and increased mortality (7-11). Even if they do not have severe consequences, they may cause a fear of walking and of leaving the house, limiting patients’ activities and independence and worsening their quality of life (QoL) (12). Previous studies showed that depression is the most important factor impairing PD patients’ QoL, and that disability, disease severity, cognitive impairment and sleep disorders also have an impact on these patients’ QoL (13-17). Moreover, it was suggested that a history of falls or of gait difficulties may also influence QoL in PD (16). In the present study we aimed to draw clinicians’ attention to falls in PD by investigating the prevalence of the different causes of falls and evaluating their influence on PD patients’ QoL, relating our findings to other factors including age, duration and progression of PD, daily levodopa dosage, cognitive dysfunction, sex, motor fluctuations, type of PD, and therapeutic regimen (monotherapy with levodopa or polytherapy with levodopa and other antiparkinsonian drugs).

Materials and methods

Patients’ characteristics
Sixty patients with probable idiopathic PD, diagnosed in conformity with Oertel and Quinn’s (18) clinical diagnostic criteria [modified from Gibb and Lees (19) and Ward and Gibb (20)], were included in the study. Patients showing atypical symptoms (including falls) in the initial period of the disease (within three years of onset of PD, or five years in the case of toppling falls) were not included to limit false positive diagnoses (21-24). Fifty-one patients were seen at the Outpatient Clinic of the Department of Neurology and Epileptology of the Medical Center for Postgraduate Education in Warsaw (Poland) and nine patients in the Outpatient Clinic of the Department of Neurology of the Jagiellonian University in Cracow (Poland). No significant differences were found between the two populations. Patients had to give their informed consent. In the total sample of 60 patients (31 women and 29 men) the mean age was 67.77 (range 42-82, SD 10.35) years and the mean disease duration was 8.00 (range 1-25, SD 5.11) years. The tremulous type of PD was found in five patients, the akinetic-hypertonic type in 17, and the mixed type in 38. Fifty-five patients were taking levodopa at a mean daily dosage of 690.45 mg (range 100-2125, SD 408.12). Of these, 24 were in monotherapy with levodopa and 31 in polytherapy with levodopa and other antiparkinsonian drugs (se-
legible, bromocriptine, pergolide or amantadine). Of the five patients not taking levodopa, two were on other antiparkinsonian drugs and three were not under any treatment at entry to the study. The mean levodopa daily dosage was 744.79 mg (range 100-2125, SD 462.80) in the monotherapy group and 648.39 mg (range 100-1500, SD 362.51) in the polytherapy group. No significant differences in sex, age and type of disease were observed between the two groups (monotherapy and polytherapy). Thirty-one patients (14 women, 17 men) had falls and 29 (17 women, 12 men) did not report falls. In the first group, falls had begun in the 6 months prior to entering the study. The total number of falls reported by patients was between one and five, with the exception of one person who suffered from several to more than ten falls daily. The mean age of the patients in the group with falls was 68.74 years (range 45-83, SD 10.07) and the mean disease duration was 9.61 years (range 3-25, SD 5.49), versus 66.72 (range 42-82, SD 10.73) and 6.29 (range 1-16, SD 4.10) in the group of patients without falls. There were no significant differences between the groups in sex, age and type of disease.

Analysis of causes of falls

Data from interview (standardized and conducted by a neurologist in the presence of a caregiver), and the findings of a physical examination and of the various investigations were analyzed to ascertain the cause of falls. Falls were considered to be due to postural instability when a patient reported falls occurring during changes of position and when physical examination revealed abnormal postural responses and “pull test” results. The falls were considered to be due to freezing or festination in patients who reported that their steps got shorter and that they bent on walking. In patients who fell down on standing, experiencing a sensation of lightheadedness, and who gave a positive Schellong, the cause of falls was classified as symptomatic orthostatic hypotension. Toppling falls were diagnosed in patients who reported a tendency to fall heavily, like a log, from a standing position with no apparent cause (although we first excluded vertebr-basilar insufficiency and impaired circulation in the ultrasonography of carotid and vertebral arteries, to distinguish these falls from drop attacks). Falls caused by non-parkinsonian neurological deficits (cerebellar, vestibular and visual disorders, paresis, etc.) were diagnosed by interview, physical examination and additional investigations (cervical X-ray, carotid and vertebral artery ultrasonography, computed tomography or magnetic resonance imaging, laryngological and ophthalmological examinations). In cases in which the falls were, in fact, syncopes, and ECG and Holter monitoring revealed impaired action of the heart, they were categorized as due to cardiac causes. The falls were classified as due to environmental causes when they were related to incorrect shoes, incorrect use of ambulation aids, etc.

Statistical analysis

Mean values were compared using a multiple-way analysis of variance (ANOVA) and distributions were analyzed using the Chi-square test with Yates’ correction and the Mann-Whitney test. Pearson’s linear correlation analysis and multiple regression analysis were used to determine the relationship between QoL and age, disease duration, disease progression, and impairment of cognitive function. The level of statistical significance was set at p<0.05.

Results

Disease progression, clinical status, motor fluctuations, cognitive dysfunction, EEG, asymptomatic orthostatic hypotension and QoL (in the whole sample)

Of the total sample of 60 patients, five (8.3%) were in stage 1, twenty (33.3%) in stage 2, twenty-six (43.3%) in stage 3, eight (13.3%) in stage 4, and one (1.8%) in stage 5 of the Hoehn and Yahr scale calculated in the “on” period. The mean UPDRS score was 45.43 (range 12-98, SD 21.82), also calculated in the “on” period. Twenty-nine patients had motor fluctuations with a mean UPDRS score of 32.76 (range 12-53, SD 12.37) in the “on” period and 55.79 (range 27-102, SD 17.82) in the “off” period. Thirty-one patients had no motor fluctuations with a mean UPDRS score of 57.29 (range 20-98, SD 22.20). These two groups differed in their mean daily dosage of levodopa: 753.45 mg (range 0-2125, SD 492.29) in the group with motor fluctuations versus 520.16 mg (range 0-1200, SD 345.45) in the group without (F=4.56, p<0.05). No difference was found in age, sex, disease duration, disease progression, or cognitive dysfunction. The mean MMSE score was 25.90 (SD 3.55). Forty-three (71.7%) patients had a score of over 24 (no cognitive dysfunction) and 17 (28.3%) patients had a score equal to or lower than 24 (cognitive dysfunction). There was no difference between these two groups in age, sex, duration of the disease, or its progression. An abnormal EEG was found in forty patients (66.7%). Generalized slowing of back-
ground activity was found in twenty-one patients (35.0%), occasional alterations (theta waves in frontal regions) in seventeen (28.3%) and paroxysmal theta or sharp waves in two (3.3%). The Schellong test revealed symptomatic orthostatic hypotension in five patients, of whom two reported falls. The mean PDQ-39 Summary Index was 32.17 (SD 16.82). The mean subscores were highest in the domains of emotional wellbeing (x̅=39.09, SD 22.16), bodily discomfort (x̅=38.30, SD 22.09), activities of daily living (x̅=36.82, SD 27.06), stigma (x̅=36.32, SD 25.31) and mobility (x̅=26.20, SD 25.46) (Fig. 1).

Analysis of causes of falls (in the 31 patients with falls)

It was found that nine of the 31 patients reporting falls (29%) fell because of postural instability, eight (25.8%) because of freezing or festinations, and one patient (3.2%) because of symptomatic orthostatic hypotension; eight patients (25.8%) had toppling falls, two patients (6.5%) fell because of non-parkinsonian neurological deficits (vertebro-basilar insufficiency in patients with cervical spondylosis), and two (6.5%) due to cardiac causes (heart arrhythmia requiring implantation of pacemaker). The cause of falls could not be determined in one patient (3.2%) (epilepsy and cardiac disorders were excluded). None of patients fell due to levodopa-induced dyskinesia or environmental causes. No patient had more than one type of falls.

Comparison of patients with and without falls

Patients with and those without falls differed in disease duration (F=6.97, p<0.01), daily dosage of levodopa (F=4.38, p<0.05), disease progression (Z=2.08, p<0.05), proportion of abnormal EEG (χ²=5.64, p<0.05), and quality of life (F=39.28, p<0.01). The mean disease duration was 9.61 (SD 5.49) years and the mean daily dosage of levodopa was 743.55 mg (SD 393.86) in the group with falls versus 6.29 years (SD 4.10) and 514.66 mg (SD 452.80) in the group without falls. Patients with falls had a more advanced stage of PD, assessed using the Hoehn and Yahr scale, and more frequently presented abnormalities in EEG. Abnormal EEG was found in twenty-five (80.4%) of the patients with falls versus fifteen (51.7%) of those without falls. The most frequent abnormality in the group with falls was generalized slowing of background activity, found in eighteen (58.1%) of these subjects; in the group without falls it was occasional theta waves in frontal regions, found in twelve (41.4%) of these subjects (Fig.s 2 and 3).

Qol assessed by PDQ-39 was significantly worse in the patients with falls in all eight domains, but particularly in the domains of mobility and activities of daily living (Fig. 4). No significant differences emerged between the group with falls and the group without falls in motor fluctuations, cognitive dysfunction and results of the Schellong test.

Figure 1 - Investigated patients’ quality of life. Domains of quality of life assessed by PDQ-39: a=mobility; b=activities of daily living; c=emotional wellbeing; d=stigma; e=social support; f=cognition; g=communication; h=bodily discomfort; i=PDQ-39 summary index.

Figure 2 - Electroencephalography (EEG) in the group of patients with falls. Abbreviations: a=normal EEG; b=generalized slowing of background activity; c=occasional alterations (theta waves in frontal regions); d=paroxysmal theta or sharp waves.

Figure 3 - Electroencephalography (EEG) in the group of patients without falls. Abbreviations: a=normal EEG; b=generalized slowing of background activity; c=occasional alterations (theta waves in frontal regions).

Figure 4 - Patients’ quality of life in the group with falls versus the group without falls. Domains of quality of life assessed by PDQ-39: a=mobility; b=activities of daily living; c=emotional wellbeing; d=stigma; e=social support; f=cognition; g=communication; h=bodily discomfort; i=PDQ-39 summary index; f=value of the ANOVA multiple-way analysis of variance.
Influence of age, disease duration, disease progression, daily levodopa dosage and cognitive dysfunction on patients' QoL (in the whole sample)

Pearson’s linear analysis showed a significant correlation between the patients’ QoL and disease duration, disease progression, daily levodopa dosage, and impairment of cognitive function. However, this correlation was not found for all the QoL domains assessed by PDQ-39. No relationship was found between the dimensions emotional wellbeing, stigma and bodily discomfort and the investigated factors. Correlations between QoL assessed by PDQ-39 and the studied factors are given in Table I. The correlation coefficients, though statistically significant, were not high (mainly between 0.3 and 0.5); multiple regression analysis was used to determine the relationship between the QoL and factors that had showed significant correlation on the Pearson's linear analysis. The model explained 19% of the variance of the PDQ-39 Summary Index (adjusted R²=0.19). Duration of the disease and impairment of cognitive function contributed to the model (p<0.05). The model also explained 41% of variance of the QoL in activities of daily living (adjusted R²=0.41), 14% of the variance in social support (adjusted R²=0.14), 13% of the variance in cognition (adjusted R²=0.13), and 14% of the variance in communication (adjusted R²=0.14). QoL in activities of daily living depended on the duration of the disease (p<0.05), its progression (p<0.01) and daily levodopa dosage (p<0.05), whereas QoL in social support depended on daily levodopa dosage and impairment of cognitive function (p<0.05), and QoL in cognition and communication on impairment of cognitive function (p<0.01, and p<0.05) (Table II).

Table I - Correlations between quality of life assessed by PDQ-39 and studied factors.

<table>
<thead>
<tr>
<th>Domains of quality of life</th>
<th>Age</th>
<th>Disease duration</th>
<th>Disease progression</th>
<th>Levodopa dosage</th>
<th>Cognitive dysfunction</th>
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</thead>
<tbody>
<tr>
<td>Mobility</td>
<td>p=ns</td>
<td>r=0.36</td>
<td>r=0.35</td>
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<tr>
<td>Activities of daily living</td>
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<td>r=0.52</td>
<td>r=0.50</td>
<td>r=0.30</td>
<td>p=ns</td>
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<tr>
<td>Emotional wellbeing</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
</tr>
<tr>
<td>Stigma</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
</tr>
<tr>
<td>Social support</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>r=0.27</td>
</tr>
<tr>
<td>Cognition</td>
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<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>r=0.45</td>
</tr>
<tr>
<td>Communication</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>r=0.33</td>
</tr>
<tr>
<td>Bodily discomfort</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
</tr>
<tr>
<td>PDQ-39 Summary Index</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
</tr>
</tbody>
</table>

Abbreviations: r=Pearson’s linear correlation coefficient; ns=not significant.

Table II - Results of the multiple regression analysis.

<table>
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<tr>
<th>Domains of quality of life</th>
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<th>Disease progression</th>
<th>Levodopa dosage</th>
<th>Cognitive dysfunction</th>
<th>Values of the model</th>
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</thead>
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<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
</tr>
<tr>
<td>Activities of daily living</td>
<td>β=0.27</td>
<td>β=0.36</td>
<td>β=0.25</td>
<td>p=ns</td>
<td>F=7.90</td>
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<td></td>
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<td>p&lt;0.01</td>
<td>p&lt;0.05</td>
<td>R²=0.41</td>
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<tr>
<td>Emotional wellbeing</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
</tr>
<tr>
<td>Stigma</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
</tr>
<tr>
<td>Social support</td>
<td>p=ns</td>
<td>p=ns</td>
<td>β=0.34</td>
<td>β=0.28</td>
<td>F=2.57</td>
</tr>
<tr>
<td></td>
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<td>p&lt;0.05</td>
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<tr>
<td>Cognition</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>β=0.44</td>
<td>F=2.43</td>
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<td>p&lt;0.01</td>
<td>R²=0.13</td>
</tr>
<tr>
<td>Communication</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>β=0.30</td>
<td>F=2.61</td>
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<tr>
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<td></td>
<td></td>
<td>p&lt;0.05</td>
<td>R²=0.14</td>
</tr>
<tr>
<td>Bodily discomfort</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
<td>p=ns</td>
</tr>
<tr>
<td>PDQ-39 Summary Index</td>
<td>β=0.30</td>
<td>p=ns</td>
<td>p=ns</td>
<td>β=0.28</td>
<td>F=3.29</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.05</td>
<td></td>
<td></td>
<td>p&lt;0.01</td>
<td>R²=0.19</td>
</tr>
</tbody>
</table>

Abbreviations: β=regression coefficient; R²=adjusted coefficient of determination; F=value of the analysis; ns=not significant.
**Falls in Parkinson’s disease**

**Influence of sex, motor fluctuations, type of disease, and monotherapy versus polytherapy on patients’ QoL**

Men had worse QoL only in social support (F=4.56, p<0.05). The mean score in this domain was 20.90 (SD 25.65) in men versus 9.64 (SD 13.79) in women. Sex had no influence either on the other QoL domains assessed by PDQ-39 or on the PDQ-39 Summary Index. Motor fluctuations, type of PD, and therapeutic regimen (monotherapy with levodopa or polytherapy with levodopa and other antiparkinsonian drugs) also had no influence on patients’ QoL.

**Discussion**

This study confirmed the variety of the causes of falls in PD and the need for an individual approach to this problem. Most frequently, patients fell due to postural instability, freezing or festinations, and sudden loss of postural reflexes (toppling falls). The causes of falls were treatable (with varying degrees of efficacy) in more than 50% of our patients. In cases of freezing or festinations and orthostatic hypotension, patients may benefit from modification of antiparkinsonian pharmacotherapy and education about specific behaviors (5). Falls due to other neurological and medical disorders can also be limited by appropriate management. In particular, the implantation of a pacemaker in a case of heart arrhythmia may prevent falls that are, in fact, syncopes, which occurred in two of our patients. Disorders of the sympathetic system affecting the myocardium can be responsible for arrhythmia in PD patients (30,31). Given that routine diagnostic methods may fail to detect this arrhythmia, it is likely that it may cause falls in PD patients more often than is thought to be the case. Postural instability, the most frequent cause of falls (reported in 29% of cases) do not usually respond to antiparkinsonian pharmacotherapy but may be limited by physical therapy, gait training and learning of specific behaviors (the correct way to rise from a chair, to turn, etc.) (5). Sudden loss of postural reflexes (resulting in toppling falls), on the other hand, is not an independent risk factor, since it depends on the duration and progression of the disease. It is known that EEG abnormalities occur more often in PD patients than in older people without PD and that these alterations (mainly generalized slowing of background activity) affect 35-75% of PD patients (32), which is in line with the findings of the present study (66.7% in all patients but 80.6% in the group with falls and 51.7% in the group without falls). As expected, generalized slowing of background activity was predominant but only in the group with falls, whereas in the group without falls occasional alterations (theta waves in frontal regions) prevailed. This difference, as well as the higher prevalence of EEG abnormalities in patients with falls, could be explained by the PD progression. Our study showed that quality of life was negatively influenced by the incidence of falls in all domains assessed by PDQ-39, but mostly in those of mobility and activities of daily living. However, in a patient self-evaluation, falls were found to influence not only, as expected, mobility, activities of daily living, emotional wellbeing and stigma, but also social support, cognition, communication and bodily discomfort (including feeling of pain). Other factors studied did not show this multidirectional impact on the patients’ QoL. We stated that cognitive dysfunction influenced QoL in the PDQ-39 domains of cognition, social support and communication; disease duration and progression only in that of activities of daily living, and levodopa daily dosage in those of activities of daily living and social support. The sex-related differences in the patients’ QoL were also limited, QoL being worse in men only in the domain of social support. We found no influence of age, motor fluctuations, type of disease or medication regimens (levodopa monotherapy or polytherapy with levodopa and other antiparkinsonian drugs) on the patients’ QoL.

The effect of levodopa dosage on patient QoL seemed surprising, but may be explained by the fact that levodopa dosage depended on disease duration and progression, both factors that (when longer and more advanced) are associated with more frequent drug administration and incidence of late levodopa complications. On the other hand, the lack of influence of therapeutic regimen (levodopa monotherapy versus polytherapy with levodopa and other antiparkinsonian drugs: selegiline, bromocriptine, pergolide or amantadine) was predictable, supporting the view that levodopa is still the most effective antiparkinsonian drug, whereas the main justification for polytherapy is to limit late levodopa complications.

Our study results, emphasizing the influence of falls on PD patients’ QoL, may have practical implications for PD management since they underline the need to diagnose the causes of falls and to institute appropriate treatment.

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