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ORIGINAL ARTICLE

Impact of autonomic dysfunctions on the quality of life in Parkinson's disease patients

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Abstract Autonomic dysfunctions are part of a spectrum of non-motor symptoms in Parkinson's disease (PD) patients. The aim of the study was to assess the prevalence of autonomic dysfunctions and their influence on the quality of life (QoL) in PD patients, adjusted for age, sex, disease duration and motor symptoms. Patients were evaluated for motor function (Unified Parkinson's Disease Rating Scale, UPDRS part III), disease stage (Hoehn and Yahr scale, H&Y scale), autonomic dysfunction (Scales for Outcomes in Parkinson's disease, Autonomic, SCOPA-AUT) and QoL (Parkinson's Disease Questionnaire-39, PDQ-39). Urinary, gastrointestinal and sexual autonomic dysfunctions were most frequently reported, while the most severe symptoms were reported for sexual and urinary systems. Age and motor symptoms did not correlate with autonomic dysfunction, while disease duration correlated with cardiovascular dysfunction. There were sex differences on the thermoregulation subscale. All types of autonomic dysfunction influenced QoL, mostly gastrointestinal and thermoregulatory dysfunctions, except for sexual one. Many aspects of QoL (activity of daily living, emotion, cognitive functions, communication and social support) except for stigma and mobility were affected by autonomic dysfunctions. Age, disease duration, sex and motor symptoms were not found to affect global QoL scores, but had detrimental effects on different PDQ-39 dimensions. Autonomic dysfunctions influence QoL in more aspects than motor symptoms, age, disease duration and sex. Patients tend to be more stigmatized with motor than non-motor symptoms.

Keywords Autonomic dysfunctions · Parkinson's disease · Quality of life · SCOPA-AUT · PDQ-39

Introduction

Autonomic dysfunctions (AD) are part of a spectrum of non-motor symptoms in Parkinson's disease (PD) patients. These include urinary, gastrointestinal, sexual, cardiovascular, visual and thermoregulation system involvement [1]. Their prevalence ranges between 14 and 80% [2]. Some of them can occur even in the premotor or early stage of the disease, while some symptoms tend to occur in the advanced stage of the disease [3, 4]. Gastrointestinal and urinary symptoms usually occur as earliest disorders, while cardiovascular symptoms tend to become more prominent during the course of the disease [4]. Autonomic dysfunction symptoms significantly impair the quality of life (QoL) scores in PD patients, even more than motor symptoms [2, 5, 6]. The aim of the study was to assess the prevalence of autonomic dysfunctions and their influence on QoL adjusted for age, sex, disease duration and motor symptoms in our group of PD patients.

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Patients and methods

The study included patients with idiopathic Parkinson's disease (IPD) consecutively recruited from an outpatient movement disorder clinic at Osijek University Hospital Center. Inclusion criterion was IPD diagnosis according to the UK brain bank criteria [7], either in early or advanced stage of the disease. Exclusion criterion was a specific treatment option for advanced PD (Duodopa gel, apomorphine, deep brain stimulation). We did not exclude demented or depressed patients but we used clinical judgment to choose those patients that were capable to fill out the questionnaires. Prior to study entry, they provided their informed consent and the study was approved by the Hospital Ethics Committee. Patients were evaluated for demographic data including age, sex and disease duration, motor symptoms (Unified Parkinson Disease Rating Scale part III, UPDRS III), disease stages (Hoehn and Yahr scale, H&Y scale), autonomic functions (Scales for Outcomes in Parkinson's Disease-Autonomic, SCOPA-AUT) and QoL (Parkinson's Disease Questionnaire-39, PDQ-39). The SCOPA-AUT consists of 25 items assessing the following regions: gastrointestinal (7), urinary (6), cardiovascular (3), thermoregulatory (4), pupillomotor (1), and sexual (2 items for men and 2 items for women) dysfunction. Each subscale score is divided by maximal subscale score and the result is presented on a 1–100 scale. Higher score denotes worse symptoms [8]. The PDQ-39 consists of 39 questions divided into 8 parts scoring many aspects of life: mobility, activity of daily living, emotional state, stigma, social support, cognitive function, communication and body discomfort. Each question is scored 0–4 points, ranging from 0—best to 4—worst. The score is divided by maximal score and the result is presented on a 0–100 scale. Higher score denotes worse symptoms [9].

On statistical analysis, we used SPSS for Windows ver. 8 (SPSS Inc., Chicago, IL, USA). Relative and absolute frequency was used for categorical data. Numerical results were expressed as mean and standard deviation (and if not normally distributed, as median and interquartile range). Distribution of numerical variables was tested using Kolmogorov–Smirnov test. Correlation was tested using Pearson coefficient of correlation for normal distribution and Spearman coefficient of correlation for data that did not have normal distribution. Differences between independent groups were tested with parametric Student's t test or nonparametric Mann–Whitney U test. The level of significance was set at $p < 0.05$.

Results

We analyzed 40 patients, 27 male and 13 female, mean age 67.2 and mean disease duration 5 years. The mean UPDRS III score was 17.7 (range 2–63) and most of the patients (92.5%) had mild disease stage (H&Y scale 0–2.5). The most frequently reported autonomic dysfunctions were urinary (100%), followed by gastrointestinal and sexual (95%), thermoregulatory (77.5%), cardiovascular (62.5%) and visual (50%) disorders. Most affected autonomic dysfunctions were urinary and sexual (SCOPA-AUT score 33.34), followed by thermoregulation (25), cardiovascular (22.23), gastrointestinal (19.05) and visual (16.67) dysfunctions. Correlation between each autonomic function and PDQ-39 yielded statistically significant results for almost all autonomic dysfunctions except for sexual one (Table 1). Correlation between SCOPA-AUT and aspects of life measured with PDQ-39 revealed statistically significant results for activity of daily living, emotional well-being, social support, cognitive functions, communication and body discomfort, but not for stigma and mobility (Table 2). UPDRS part III and age did not correlate with any subscale of SCOPA-AUT or with total SCOPA-AUT score, while disease duration negatively correlated with cardiovascular symptoms ($r = -0.331$; $p = 0.037$). Significant sex differences were found for thermoregulatory function. Females most often reported problems with this autonomic function ($t = 0.052$; $p = 0.018$) (Table 3). Comparison of PDQ-39 and UPDRS part III results yielded significant correlation for the subscales of stigma ($r = 0.404$; $p = 0.011$) and communication ($r = 0.367$; $p = 0.022$). Age negatively correlated with body discomfort ($r = -0.460$; $p = 0.003$), while disease duration correlated significantly with stigma ($r = 0.426$; $p = 0.007$) and cognitive function ($r = -0.341$; $p = 0.034$). Sex differences were noticed in two fields of QoL. Female patients more often reported difficulties in mobility ($t = 0.687$; $p = 0.020$) and emotional well-being ($t = 0.087$; $p = 0.048$) (Table 4).

Discussion

Forty patients with idiopathic PD were analyzed for AD and QoL. Gastrointestinal, sexual and urinary dysfunctions were most frequently present, while the most severe

Table 1 Correlation between autonomic symptoms and PDQ-39

	PDQ-39 (ρ)	p
Gastrointestinal	0.678	<0.001**
Urinary	0.366	0.024*
Cardiovascular	0.435	0.006**
Visual	0.468	0.003**
Thermoregulation	0.523	0.001**
Sexual	−0.010	0.970

PDQ-39 Parkinson's Disease Questionnaire-39

* $p < 0.05$; ** $p < 0.01$

Table 2 Correlation between PDQ-39 subscales and SCOPA-AUT

	SCOPA-AUT (ρ)	p
Mobility	0.303	0.061
Activity of daily living	0.515	0.001**
Emotion	0.421	0.008**
Stigma	0.079	0.632
Social support	0.364	0.023*
Cognitive functions	0.400	0.012*
Communications	0.326	0.043*
Physical discomfort	0.636	<0.001**

SCOPA-AUT Scales for Outcomes in Parkinson's Disease—Autonomic, *PDQ-39* Parkinson's Disease Questionnaire-39

* $p < 0.05$, ** $p < 0.01$

symptoms were reported for sexual and urinary systems. Jost found that gastrointestinal, urogenital and cardiovascular dysfunctions were predominant in PD patients, while Golab-Janowska et al. report on sexual, urinary, gastrointestinal and seborrhea as the most frequent ADs in PD [2, 10]. Sakakibara et al. analyzed sexual function in 46 men with PD (age 35–70) and 258 healthy men (age 30–70) as control group. The prevalence of dysfunction was significantly higher in PD patients as compared with control group. In the majority of patients, the onset of sexual dysfunction followed the appearance of motor disorder [11].

Analyzing the influence of disease duration on AD, we found cardiovascular symptoms to have occurred more often in patients with shorter disease duration. Some studies report that cardiovascular symptoms correlate with disease duration and tend to occur in advanced disease stage, while others report that sympathetic dysfunctions appear in early stage of the disease in treatment-naive patients or even precede motor symptoms [4, 12, 13]. We did not analyze the possible effect of therapy (levodopa-equivalent daily dose (LEDD) and antihypertensive treatment) or comorbidity on orthostatic hypotension, which may, in part, explain the negative correlation between disease duration and cardiovascular dysfunction.

According to literature data, age does not influence development of AD [14], which is consistent with our results. In addition to age, we found it for motor symptoms as well. Analyzing the impact of sex on AD, we found

Table 3 Correlation between autonomic symptoms and UPDRS part III, age, disease duration and sex

	UPDRS part III		Age		Disease duration		Sex	
	(r)	p	(r)	p	(r)	p	t	p
Gastrointestinal	0.066	0.685	0.091	0.578	−0.055	0.734	0.220	0.256
Urinary	0.238	0.144	−0.255	0.117	−0.196	0.233	0.455	0.770
Cardiovascular	−0.019	0.907	−0.237	0.141	−0.331	0.037*	0.959	0.153
Visual	0.024	0.885	−0.096	0.556	−0.227	0.159	0.209	0.350
Thermoregulation	0.037	0.819	−0.161	0.321	−0.031	0.849	0.052	0.018*
Sexual	−0.038	0.882	0.285	0.252	0.464	0.052	0.640	0.606
Total	−0.085	0.602	−0.049	0.763	−0.151	0.353	0.240	0.585

UPDRS part III Unified Parkinson's Disease Scale part III

* $p < 0.05$

Table 4 Correlation between PDQ-39 subscales and UPDRS part III, age, disease duration and sex

	UPDRS part III		Age		Disease duration		Sex	
	(r)	p	(r)	p	(r)	p	t	p
Mobility	0.203	0.216	−0.100	0.546	0.164	0.320	0.687	0.020*
Activity of DL	0.154	0.351	−0.114	0.490	0.152	0.357	0.733	0.288
Emotion	0.266	0.102	−0.253	0.120	−0.120	0.467	0.087	0.048*
Stigma	0.404	0.011*	−0.058	0.725	0.426	0.007**	0.482	0.789
Social support	0.053	0.749	−0.230	0.160	0.061	0.711	0.489	0.381
Cognition	0.072	0.663	−0.039	0.816	−0.341	0.034*	0.978	0.892
Communications	0,367	0.022*	−0.220	0.179	0.193	0.238	0.635	0.062
Discomfort	−0.009	0.956	−0.460	0.003**	−0.070	0.673	0.317	0.192
Total	0.268	0.098	−0.230	0.158	0.084	0.610	0.243	0.057

UPDRS part III Unified Parkinson's Disease Scale part III, *Activity of DL* activity of daily living

* $p < 0.05$; ** $p < 0.01$

female patients to have reported problems with thermoregulation more often than male patients.

Almost all ADs influenced QoL, mostly gastrointestinal and thermoregulatory dysfunctions, except for sexual one. This could be explained by older age of the patients (mean age 67.2 years) with less interest in sexual intercourse, making this symptom not much relevant for QoL. Comparing the results among four age subgroups (subjects in their 30s, 40s, 50s and 60s) in control group, Sakakibara et al. found the frequency of sexual intercourse and orgasm to be significantly lower in older individuals [11]. The QoL scores correlated most strongly with AD, particularly urinary and gastrointestinal symptoms [15]. Gallagher et al. report on health-related QoL to be influenced by thermoregulatory, gastrointestinal and cardiovascular autonomic function (especially orthostatic hypotension) and urinary problems [16]. Even asymptomatic patients with orthostatic hypotension showed similar impairment in PDQ-8 (shorter version of PDQ-39) as symptomatic one [17]. Sweating disturbances are common and distressing symptoms of PD that are related mainly to AD, off periods, and dyskinesias, but Swinn et al. found that sweating disturbances did not correlate with overall QoL scores, although many patients reported physical, social and emotional impairment due to sweating [18].

Many aspects of QoL (activity of daily living, emotion, cognitive functions, communication and social support) except for stigma and mobility were affected by ADs; however, body discomfort was the most pronounced. Age, disease duration, sex and motor symptoms were not found to affect global QoL scores, but had detrimental effects on different PDQ-39 dimensions. Our female patients gave significantly more negative assessment of their QoL than men in the aspects of mobility and emotional well-being. Hristova et al. report that female patients had worse QoL than males in the aspects of mobility, emotional well-being, social support and bodily discomfort [19]. Patients with severe motor symptoms and longer disease duration were more stigmatized, while cognitive dysfunctions impaired QoL more often in patients with shorter disease duration. Patients with severe motor symptoms also had worse QoL due to the problems with communication, while body discomfort impaired QoL more often in younger patients.

Our study suffered from some limitations. We did not analyze LEDD, concomitant medications or comorbidities that could influence AD. It is known that dopaminergic therapy lowers blood pressure, while polyneuropathy, prostate problems, cardiovascular and cerebrovascular diseases lead to many ADs. Small sample size also limited the strength of our conclusions; so, the results should be interpreted with caution.

Conclusion

Urinary, gastrointestinal and sexual dysfunctions are the most common ADs, and urinary and sexual dysfunctions are most severe in presentation. All ADs except for sexual AD have an adverse impact on QoL. All aspects of QoL except for stigma and mobility are disrupted, with physical discomfort being most pronounced. Age, disease duration, sex and motor symptoms were not found to affect global QoL scores, but had detrimental effects on different PDQ-39 dimensions. ADs influence QoL in more aspects than motor symptoms, age, disease duration and sex. Patients tend to be more stigmatized with motor than non-motor symptoms.

Compliance with ethical standards

Conflict of interest Author A received honoraria from Fresenius d.o.o., Pliva Hrvatska d.o.o., Medis d.o.o; and received financial support for attending symposia from Abbvie d.o.o. and Medis d.o.o. Authors B, C and D have no conflict of interest. Author E received honoraria from Novartis.

Ethical standards The study was approved by the Hospital Ethics Committee.

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Informed consent Prior to study entry, they provided their informed consent.

References

1. Micieli G, Tosi P, Marcheselli S, Cavallini A (2003) Autonomic dysfunction in Parkinson's disease. Neurol Sci 24(1):S32–S34
2. Jost WH (2003) Autonomic dysfunctions in idiopathic Parkinson's disease. J Neurol 250(1):i28–i30
3. Li K, Reichmann H, Ziemssen T (2015) Recognition and treatment of autonomic disturbances in Parkinson's disease. Expert Rev Neurother 15(10):1189–1203
4. Liepelt-Scarfone I, Pilotto A, Müller K, Bormann C, Gauss K, Wurster I, Streffer J, Berg D (2015) Autonomic dysfunction in subjects at high risk for Parkinson's disease. J Neurol 262(12):2643–2652
5. van Uem JM, Marinus J, Canning C, van Lummel R, Dodel R, Liepelt-Scarfone I, Berg D, Morris ME, Maetzler W (2015) Health-related quality of life in patients with Parkinson's—a systematic review based on the ICF model. Neurosci Biobehav Rev 61:26–34
6. Prakash KM, Nadkarni NV, Lye WK, Yong MH, Tan EK (2016) The impact of non-motor symptoms on the quality of life of Parkinson's disease patients: a longitudinal study. Eur J Neurol 23(5):854–860
7. Hughes AJ, Daniel SE, Kilford L, Lees AJ (1992) Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 55:181–184
8. Visser M, Marinus J, Stiggelbout AM, Van Hilten JJ (2004) Assessment of autonomic dysfunction in Parkinson's disease: the SCOPA-AUT. Mov Disord 19(11):1306–1312

9. Hagell P, Nygren C (2007) The 39 item Parkinson's Disease Questionnaire (PDQ-39) revisited: implications for evidence based medicine. J Neurol Neurosurg Psychiatry 78:1191–1198
10. Gołab-Janowska M, Budzianowska A, Honczarenko K (2011) Autonomic disorders in Parkinson's disease. Ann Acad Med Stetin 57(1):11–15
11. Sakakibara R, Shinotoh H, Uchiyama T et al (2001) Questionnaire-based assessment of pelvic organ dysfunction in Parkinson's disease. Auton Neurosci 92(1–2):76–85
12. De Luka SR, Svetel M, Pekmezović T, Milovanović B, Kostić VS (2014) When do the symptoms of autonomic nervous system malfunction appear in patients with Parkinson's disease? Vojnosanit Pregl 71(4):346–351
13. Goldstein DS (2014) Dysautonomia in Parkinson disease. Compr Physiol 4(2):805–826
14. van Rooden SM, Verbaan D, Stijnen T, Marinus J, van Hilten JJ (2016) The influence of age and approaching death on the course of nondopaminergic symptoms in Parkinson's disease. Parkinsonism Relat Disord 24:113–118
15. Chaudhuri KR, Healy DG, Schapira AH (2006) Nonmotor symptoms of Parkinson's disease: diagnosis and management. Lancet Neurol 5(3):235–245
16. Gallagher DA, Lees A, Schrag A (2010) What are the most important nonmotor symptoms in patients with Parkinson's disease and are we missing them? Mov Disord 25(15):2493–2500
17. Merola A, Romagnolo A, Rosso M, Lopez-Castellanos JR, Wissel BD, Larkin S, Bernardini A, Zibetti M, Maule S, Lopiano L, Espay AJ (2016) Orthostatic hypotension in Parkinson's disease: does it matter if asymptomatic? Parkinsonism Relat Disord 33:65–71
18. Swinn L, Schrag A, Viswanathan R, Bloem BR, Lees A, Quinn N (2003) Sweating dysfunctions in Parkinson's disease. Mov Disord 18(12):1459–1463
19. Hristova DR, Hristov JI, Mateva NG, Papathanasiou JV (2009) Quality of life in patients with Parkinson's disease. Folia Med (Plovdiv) 51(4):58–64