

PREVALENCE OF NON-MOTOR SYMPTOMS IN PARKINSON'S DISEASE – AN OBSERVATIONAL STUDY

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ABSTRACT

Objectives. This study aim is to evaluate the prevalence of non-motor symptoms in Parkinson's disease

Methodology. We conducted an observational study in a prospective approach on a cohort of 70 patients admitted with a diagnosis of Parkinson's disease in the Neurology Department of the University Emergency Hospital Bucharest for pre-surgery assessment or referred for a consultation to the Outpatient Department of Neurology of the Central Military Emergency Hospital, "Carol Davila" in the last two quarters of 2007, using a technique based on questionnaire (NMSQuest).

Results. Patients included in this study were generally elderly, with a long relative history of disease. They are mostly in the moderate stage of disease and used treatment regimens with combinations of drugs. Prevalence of some non-motor symptoms according to the answers of patients in NMS questionnaire (NMSQuest), like: depression, memory impairment sleep disturbances, sexual disturbances, „light head“, constipation was statistically significant high in our group of patients.

Conclusions. Non-Motor Questionnaire (NMSQuest) can be a useful clinically tool for detecting the common non-motor symptoms in patients with Parkinson's disease. Prevalence of non-motor symptoms in Parkinson's disease is high and require further evaluation of their impact on patient's quality of life.

Keywords: Parkinson disease, non-motor symptoms, prevalence, NMSQuest

BACKGROUND

Non-motor symptoms in PD involve a multitude of functions including sleep-wake cycle regulation, cognitive function, regulation of mood and hedonistic tone, autonomic nervous system function as well as sensory function and pain perception (1). Compared with the motor symptoms of Parkinson's disease, non-motor symptoms is extremely diverse, underdiagnosed and therefore undertreated, having a negative impact on quality of life of patients with Parkinson's disease. Healthcare professionals still often ignore or perhaps chose not to discuss NMS in clinic consultations. The PDNMG has led the field and developed and validated the first self-administered screening tool to detect the presence of NMS and initiate further investigation

(the NMS Questionnaire or NMSQuest) (2). It consists of 30 items, in ten domains, derived from experiences of the multi-disciplinary PDNMG (Parkinson's disease non-motor group) members, published literature, patient group responses, results from a survey of over 1000 patients and caregivers carried out in the UK, and a hospital-based survey. The instrument has demonstrated good feasibility and validity in an international scenario and can be used during routine consultations to flag symptoms needing attention. (2)

SCOPE OF THIS STUDY

- to evaluate the prevalence of non-motor symptoms in patients with Parkinson's disease.

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OBJECTIVES

To achieve the goal, this study aims to answer the following questions:

- Which is the distribution of patients according to personal characteristics (age, sex, associated comorbidities)?
- Which is the distribution of patients according to clinical stage of disease (Hoehn & Yahr stages)?
- Which is the prevalence of non-motor symptoms in patients with Parkinson's disease?
- Is there any correlation between the presence of specific non-motor symptoms and the duration of disease or clinical stages of Parkinson's disease?

METHODS

We conducted an observational study in a prospective approach on a cohort of 70 patients admitted with a diagnosis of Parkinson's disease in the Neurology Department of the University Emergency Hospital Bucharest for pre-surgery assessment or referred for a consultation to the Outpatient Department of Neurology of the Central Military Emergency Hospital, „Carol Davila” in the last two quarters of 2007.

Inclusion criteria

The study included patients with a diagnosis of Parkinson's disease according to the UK Brain Bank criteria, who signed an informed consent for the study and were older than 30 years. For data collection we used a sheet-research that included:

- Personal characteristics of the patient (age, sex)
- Characteristics of the disease (age at onset, duration of disease, clinical stage Hoehn and Yahr scale, classes of antiparkinsonian drugs.)
- Prevalence and type of non-motor symptoms using the Non-Motor Questionnaire (NMS-Quest). Each patient included in the study completed alone the questionnaire NMS Quest

Statistical analysis

- Distributions were produced for all variables included in the questionnaire
- The distributions of quantitative variables were characterized by determining indicators of central tendency (mode, median, mean value) and dispersion indicators (variance,

standard deviation). To assess the degree of dispersion of observed values from the average values, the coefficient of variation (CV) was calculated (standard deviation of average weight);

- For the distributions observed values depending on two variables we tested the statistical significance of the differences observed. We used the χ^2 test, the conditions for the application of this test being fulfilled by the distributions tested. Chosen statistical significance threshold was 5% ($p < 0.05$).

RESULTS

A. Sex distribution of the patients show a predominance of males, the proportion of men being 66% (46) and the women 34% (24) (Fig. 1).

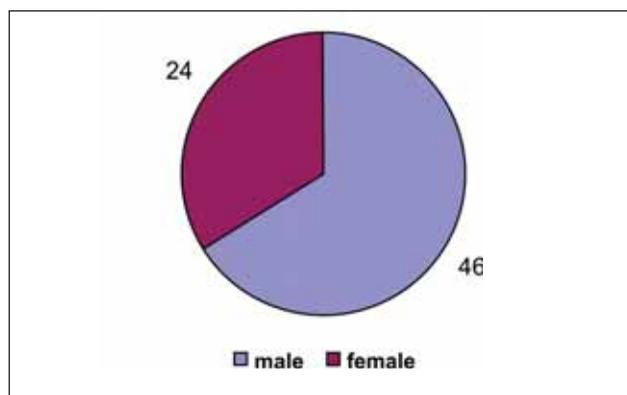


FIGURE 1. Distribution of patients by sex

B. Distribution of patients by age groups

The distribution of the patients according to age is characterized by a range of variation between 58 and 85 years with a mean age of 73.5 years accompanied by an average degree of dispersion ($sx = \pm 8$ years, $CV = 10.9\%$). 36 of the 70 patients (51.3%) were between 75 and 84 years old, with most of the patients (24) between 75-79 years old (34.3%) (Table 1, Fig. 2).

TABLE 1. Distribution of patients by group of age

Group of age (years)	No. patients	%
55-59	4	5.7
60-64	8	11.4
65-69	10	14.3
70-74	8	11.4
75-79	24	34.2
80-84	12	17.1
85-89	4	5.7
Total	70	100.0

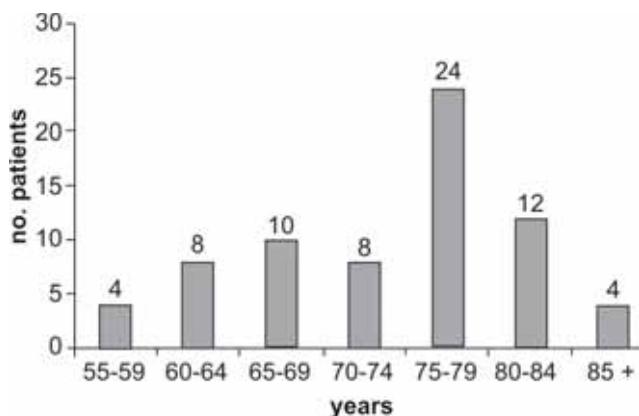


FIGURE 2. Distribution of patients by age group

C. Distribution of patients by duration of disease:

The values recorded for the variable „duration of disease” were within the range „under one year” and maximum 22 years. Therefore, the average age of disease 7.1 years is accompanied by a high degree of dispersion (sx = ± 4.5 years, CV = 63.4%). Under these conditions, the median age of disease – 6 years, would characterize the observed distribution. Most patients – 26 (37.1%) had the diagnosis of PD since 5-9 years, followed by patients with a duration of disease of 10-14 years – 22 (31.4%) (Table 2, Fig. 3).

TABLE 2. Distribution of patients by duration of disease

Duration of disease (years)	No. patients	%
0-4	20	28.6
5-9	26	37.1
10-14	22	31.4
20*24	2	2.9
Total	70	100.0

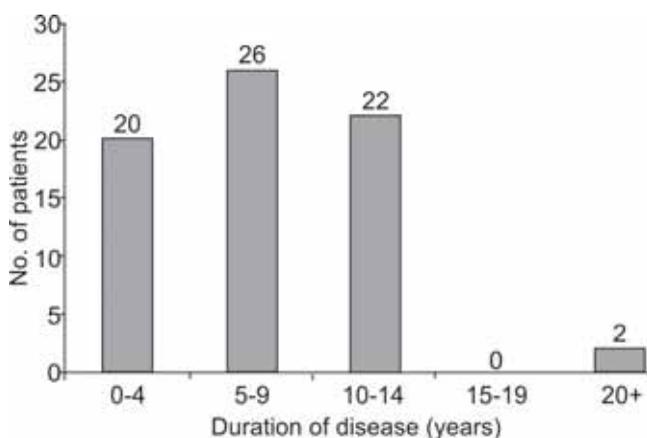


FIGURE 3. Distribution of patients by duration of disease

D. Distribution of patients by stage of disease (Hoehn & Yahr stages):

Hoehn & Yahr staging according to the distribution of the patients in this study group (see Table 3)

is characterized by an average score of 2.7 and a high degree of dispersion (sx = ± 0.7, CV = 25.9%). Under these conditions, the median score of 2.5 would better characterize the observed distribution. Modal score was 2 (20 patients – 28.6%). The scores of 2.5 and 3, respectively, were recorded at the same frequency – 18 patients each. (Fig. 4).

TABLE 3. Distribution of patients by duration of disease

Stage H&Y	No. patients	%
1.5	2	2.9
2.0	20	28.6
2.5	18	25.7
3.0	18	25.7
4.0	12	17.1
Total	70	100.0

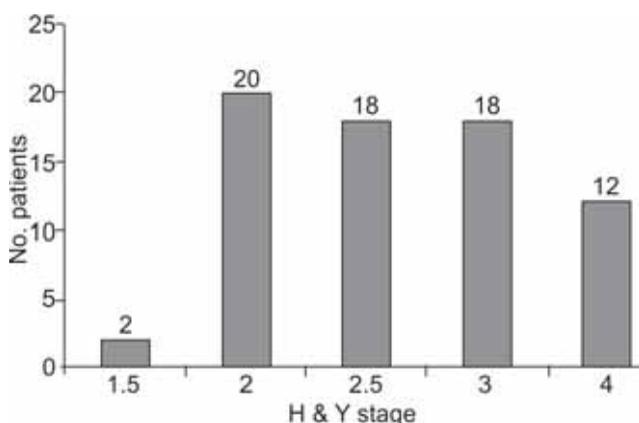


FIGURE 4. Distribution of patients by Hoehn & Yahr stage

E. Treatment – classes of drugs for the patients included in this study

The vast majority of patients in the study group, with a moderate form of the disease (Hoehn and Yahr stage 2-3), use the combined regimens with at least two classes of drugs. The most commonly used classes of antiparkinsonian drugs in the study group include the compounds of levodopa (in combination with decarboxylase inhibitors) – 64 of the 70 patients, followed by selective nonergolinic dopamine agonists – 42 out of 70 patients (Table 4).

TABLE 4. Distribution of patients by classes of medication

Treatment	No. patients
Levodopa compounds (L) + Nonergolinic dopaminergic agonists (AG)	14
L and IMAO-B	8
L+ ICOMT + AG	8
L+ ICOMT	6
L+ ICOMT+ AG + IMAO-B	6
L+ ICOMT + IMAO-B	6
L+ ICOMT +AG	6

Treatment	No. patients
AG + Amantadine (A)	4
L+ ICOMT+ AG + A+ IMAO-B	4
L	2
L+ ICOMT + A	2
L+ ICOMT + A + IMAO-B	2
L+ AG +A	2
Total	70

F. Prevalence of non-motor symptoms of Parkinson's disease:

1. Neuropsychiatric symptoms:

a) Hallucinations and delusions:

Question	Yes	No
Do you think that happens things that are not true?	4 (5.7%)	66 (94.3%)
Do you hear or see things that you know or have been told they are not there?	6 (8.6%)	64 (91.4%)

Statistically insignificant differences – Fisher test, $p = 0.50$

A small group of patients presenting hallucinations or delusions (5-8%).

b) Apathy, attention and memory:

Question	Yes	No
You have trouble remembering recent events or forget to do things?	46 (65.7%)	24 (34.3%)
Have you lost interest in what you happen around or do something	22 (31.4%)	48 (68.6%)
Do you have difficulty concentrating?	32 (45.7%)	38 (54.3%)

Statistically significant differences, $X^2_c = 8.32$, $p = 0.015$

65% of patients have recent memory impairment and about 45% report difficulty in concentration. More than one third of patients say that they have lack of interest in daily activities.

c) Depression/anxiety:

Question	Yes	No
Have you had weight changes (without changing diet)?	12 (17.1%)	58 (82.9%)
You feel sad, broken down, melancholic?	40 (57.1%)	30 (42.9%)
Do you feel anxious, scared, panicked	28 (40%)	42 (60%)

Statistically significant differences, $X^2_c = 11.95$, $p = 0.0025$

More than half of the patients (57%) had a sad, depressive mood, but the associated weight loss associated with the appetite decrease was noticed

inonly a small proportion (17%). In contrast, 40% of patients had an anxiety disorder.

2. Sleep disturbances:

Question	Yes	No
Stay awake with difficulty when you work, drive or eat?	12 (17.1%)	58 (82.9%)
Do you have difficulty falling asleep or sleeping at night?	40 (57.1%)	30 (42.9%)
Do you have vivid dreams, or nightmares?	44 (62.9%)	26 (37.1%)
Talk or move when you dream something?	24 (34.3%)	46 (65.7%)
Unpleasant sensations in the legs when you rest, needing urge to move?	28 (40%)	42 (60%)

Statistically significant differences, $X^2_c = 20.24$, $p = 0.0011$

More than half of the patients have sleep disturbances such as difficulties in falling asleep or staying asleep (57%). Approximately 63% of patients declare vivid dreams, or nightmares (but we must take into account the possible secondary reactions of the dopaminergic drugs). 40% of the patients have symptoms suggestive of „restless legs syndrome”.

3. Dysautonomy:

a) Cardiovascular symptoms:

Question	Yes	No
When rising from a chair or bed, you feel dizzy, weak, confused?	48 (68.6%)	22 (31.4%)
Fall when you stand?	16 (22.9%)	54 (77.1%)

Statistically significant differences, $X^2_c = 14.74$, $p = 0.00012$

Almost 70% of the patients declare dizziness when changing position suggesting a possible existence of orthostatic hypotension, but only 22% of patient have falls.

b) Urinary symptoms:

Question	Yes	No
When you have the feeling of urination, urgent need to get to the toilet?	48 (68.6%)	22 (31.4%)
Regularly wake up at night to go to the toilet?	58 (82.9%)	12 (17.1%)

Statistically insignificant differences, $X^2_c = 1.94$, $p = 0.16$

Almost 70% of the patients have urge to urinate and 80% of them regularly wake up at night to urinate, a result that must be analyzed taking into account the fact that the group is composed mostly of elderly men (a confounding factor being also co-

morbidity with prostatic diseases common in this group of patients).

c) Sexual function:

Of the 70 patients only 42 agreed to answer questions about sexual function.

Question	Yes	No
You have lost your interest in sexual activity ?	30 (71.4%)	12 (28.6%)
You have difficulty when you want to have sex ?	12 (28.6%)	30 (71.4%)

Statistically significant differences, $X^2_c = 7.71$, $p = 0.0054$

Among respondents, more than 70%, mostly men, report the lost of interest in sexual activity, but only 30% stating that they have difficulties in sexual relations.

d) Nonspecific dysautonomic symptoms:

Question	Yes	No
Swelling of your feet?	26 (37.1%)	44 (62.9%)
Excessive sweating?	30 (42.9%)	40 (57.1%)
You have diplopia ?	26 (37.1%)	44 (62.9%)

Statistically insignificant differences, $X^2_c = 0.32$, $p = 0.85$

Nonspecific symptoms such as excessive sweating (40% of patients), leg edema or double vision, are found less frequently in the group of patients studied.

4. Gastrointestinal symptoms:

Question	Yes	No
You have drooling of saliva during the day?	42 (60%) 28 (40%)	28 (40%) 42 (60%)
Was diminished/lost sense of taste or smell?		
Do you have difficulty swallowing food or liquids (choking when you drink or eat)?	24 (34.3%)	46 (65.7%)
You have vomiting, nausea?	18 (25.7%)	52 (74.3%)
Constipation (less than 3 bowel movements /week)?	46 (65.7%)	24 (34.3%)
Faecal incontinence?	–	70 (100.0%)
Feel the bowels not completely emptied after the toilet?	38 (54.3%)	32 (45.7%)

Statistically significant differences, $X^2_c = 17.37$, $p = 0.0038$

More than 60% of the patients have bowel disorders with constipation, more than 50% of patients requiring repeat visits to the toilet because of symptoms of „incomplete emptying of the bowel” More than 50% of the patients have drooling of saliva during daytime, sometimes very disturbing, especially in public, for the patient.

5. Pain:

When asked „Do you have unexplained pain (not due to known diseases, such as arthritis)?”, 30 patients answered affirmatively (42.9%) and 40 negative (57.1%) (Fig. 5).

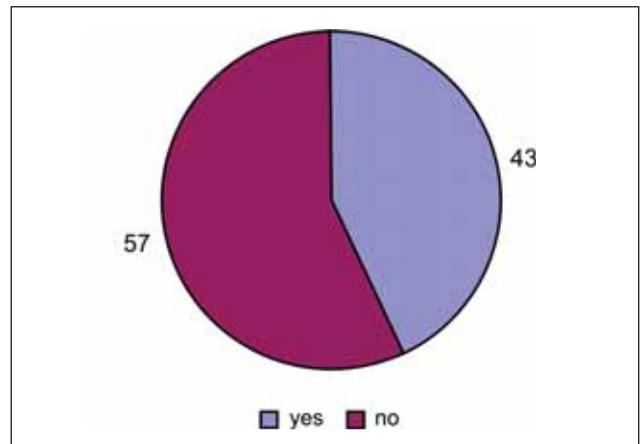


FIGURE 5. Prevalence of pain in the group (no. of patients = 70)

6. Distribution of non-motor symptoms by duration of disease

Distribution of hallucinations and delusions by duration of disease

Question	Duration of disease (years)			
	0-4	5-9	10-14	20-24
Do you think that happens things that are not true?	–	2 ↓7.7%	2 ↓9.1%	–
Do you hear or see things that you know or have been told they are not there?	2 ↓10%	2 ↓7.7%	2 ↓9.1%	–
Total	20 (28.6%)	26 (37.1%)	22 (31.4%)	2 (2.9%)

Distribution of attention, memory troubles and apathy symptoms by duration of disease

Question	Duration of disease (years)			
	0-4	5-9	10-14	20-24
You have trouble remembering recent events or forget to do things?	12 ↓60%	24 ↓92.3%	8 ↓36.4%	2
Have you lost interest in what you happen around or do something	6 ↓30%	8 ↓30.8%	6 ↓27.3%	2
Do you have difficulty concentrating?	12 ↓60%	12 ↓46.2%	6 ↓27.3%	2
Total	20 (28.6%)	26 (37.1%)	22 (31.4%)	2 (2.9%)

Since the time of diagnosis of Parkinson’s disease we meet impaired concentration and attention in this study group and there is no statistical association between their presence and duration of disease.

Distribution of anxiety and depression symptoms by duration of disease

Question	Disease duration (years)			
	0-4	5-9	10-14	20-24
Have you had weight changes (without changing diet)?	12 ↓60%	24 ↓92.3%	8 ↓36.4%	2
You feel sad, broken down, melancholic?	6 ↓30%	8 ↓30.8%	6 ↓27.3%	2
Do you feel anxious, scared, panicked	12 ↓60%	12 ↓46.2%	6 ↓27.3%	2
Total	20 (28.6%)	26 (37.1%)	22 (31.4%)	2 (2.9%)

Distribution of sleep disorders and tiredness by the duration of disease

Question	Duration of disease (years)			
	0-4	5-9	10-14	20-24
Stay awake with difficulty when you work, drive or eat?	4 ↓20%	4 ↓15.4%	2 ↓9.1%	2
Do you have difficulty falling asleep or sleeping at night?	12 ↓60%	8 ↓30.8%	18 ↓81.8%	2
Do you have vivid dreams, or nightmares?	12 ↓60%	16 ↓61.5%	16 ↓72.7%	–
Talk or move when you dream something?	10 ↓50%	8 ↓30.8%	6 ↓27.3%	–
Unpleasant sensations in the legs when you rest, needing urge to move?	10 ↓50%	8 ↓30.8%	10 ↓45.5%	–
Total	20 (28.6%)	26 (37.1%)	22 (31.4%)	2 (2.9%)

More than 60% of patients with a recent history of Parkinson’s disease have difficulty sleeping. Over the years, the percentage of those who affirm these symptoms increased in this study group to 80%.

Presence of cardiovascular dysautonomic symptoms by the duration of disease

Question	Duration of disease (years)			
	0-4	5-9	10-14	20-24
When rising from a chair or bed, you feel dizzy, weak, confused?	16 ↓80%	18 ↓69.2%	12 ↓54.5%	2
Fall when you stand?	6 ↓30%	6 ↓23.1%	2 ↓9.1%	2
Total	20 (28.6%)	26 (37.1%)	22 (31.4%)	2 (2.9%)

Symptomatic arterialhypotension may be present from the onset of the disease (more than 80% of those with a recent history of Parkinson’s disease). The analysis should also consider the factor of confusion brought by the side effects of antiparkinsonian drugs, in particular the dopamine agonist, used in most of the patients studied.

Presence of urinary symptoms according to the duration of disease

Question	Duration of disease (years)			
	0-4	5-9	10-14	20-24
When you have the feeling of urination, urgent need to get to the toilet?	14 ↓70%	22 ↓84.62%	10 ↓45.5%	2
Regularly wake up at night to go to the toilet?	18 ↓90%	24 ↓92.3%	14 ↓63.6%	2
Total	10 (28.6%)	13 (37.1%)	11 (31.4%)	1 (2.9%)

The urgency to urinate occurs in the groups of patients with a relative recent history of Parkinson’s disease (0-9 years after diagnosis) as well as frequent awakening of the patient over night, leading to severe impairment of sleep, in addition to motor symptoms of sleep.

Question	Duration of disease (years)			
	0-4	5-9	10-14	20-24
You have lost your interest in sexual activity ?	6 ↓60%	12 ↓66.7%	12 ↓85.7%	–
You have difficulty when you want to have sex ?	2 ↓20%	6 ↓33.3%	4 ↓28.6%	–
Total	5 (23.8%)	9 (42.9%)	7 (33.3%)	–

From the disease apparent clinicalonset, the patients seem to lose their interest in sexual activity (42 respondents out of the total of 70).

Presence of dysautonomic symptoms by the duration of disease

Question	Duration of disease (years)			
	0-4	5-9	10-14	20-24
Swelling of your feet?	8 ↓40%	12 ↓46.2%	4 ↓18.2%	2
Excessive sweating?	8 ↓40%	10 ↓38.5%	10 ↓45.5%	2
You have diplopia ?	10 ↓50%	14 ↓53.8%	2 ↓9.1%	–
Total	20 (28.6%)	26 (37.1%)	22 (31.4%)	2 (2.9%)

Presence of gastrointestinal symptoms by the duration of disease

Questions	Duration of disease (years)			
	0-4	5-9	10-14	20-24
You have drooling of saliva during the day?	10 ↓50%	20 ↓76.9%	10 ↓45.5%	2
Was diminished/lost sense of taste or smell?	4 ↓20%	16 ↓61.5%	6 ↓27.3%	2
Do you have difficulty swallowing food or liquids (choking when you drink or eat)?	8 ↓40%	6 ↓23.1%	8 ↓36.4%	2
You have vomiting, nausea?	4 ↓20%	8 ↓30.8%	6 ↓27.3%	–
Constipation (less than 3 bowel movements /week)?	6 ↓30%	20 ↓76.9%	18 ↓81.8%	2
Faecal incontinence?	–	–	–	–
Feel the bowels not completely emptied after the toilet?	8 ↓40%	22 ↓84.6%	6 ↓27.3%	2
Total	20 (28.6%)	26 (37.1%)	22 (31.4%)	2 (2.9%)

Constipation, the most common non-motor symptom in the group of patients studied is correlated with duration of disease (more than 80% of patients with Parkinson's disease with along history of disease affirm that)

CONCLUSIONS

In the analysis of neuropsychiatric events in this study group, we observe only a small proportion of patients who had hallucinations or delusions, 65% of patients had recent memory disturbances and about 45% reported difficulty of concentration. Since the time of diagnosis of Parkinson's disease, patients in this study group may had impaired concentration and attention and there is no statistical association between their presence and duration of disease.

More than 57% of patients had a sad mood or depression, 40% have anxiety. As noted, a minority of patients have unexplained weight changes, instead frequently interviewed patients have a combination of the two classes of symptoms (anxiety/depression), which betrays a mood disturbance in Parkinson's disease (more commonly depression than anxiety).

In this group, 57% of the patients had sleep disturbances, like difficulty in falling asleep and staying asleep, 63% of patients declare vivid dreams or nightmares. A minority of respondents have day-

time somnolence, most of them having an association between the presence of sleep disorders and of symptoms of „restless legs” or vivid dreams overnight.

Since the clinical onset of the disease, more than 60% of patients with a recent history of disease, have sleep disturbances. Over the years, the percentage of those who have these symptoms increase in this study group to 80%.

Regarding the cardiovascular symptoms in Parkinson's disease, nearly 70% of patients had dizziness when changing position, suggesting the possible existence of orthostatic arterial hypotension.

Symptomatic hypotension may be present from the clinical onset of disease (more than 80% of patients with a recent history of Parkinson's disease). The analysis must also consider the factor of confusion brought by the side effects of anti-parkinsonian drug classes.

When analyzing non-motor urinary symptoms, nearly 70% of patients had urgency to urinate and 80% of them regularly wake up at night to urinate, a result that must be analyzed taking into account the fact that the group is represented mostly by elderly men (a confounding factor may also be comorbidity with prostatic diseases common in this group of patients).

Symptoms of sexual disturbance have been less well characterized in this study group because from the 70 patients only 42 agreed to answer the questions about sexual function. Among respondents, more than 70% (mostly men) declare loss of interest in sexual activity, but only 30% stating that they have difficulties in sexual relations.

More than 60% of the patients have bowel disorder characterized by constipation, over 50% of patients requiring repeated visits to the toilet because of symptoms of „incomplete emptying of the bowels”. Over 50% of patients had drooling of saliva, sometimes very disturbing, in particular in public, for the patient. More than 40% of patients had hyposmia or ageusia. Faecal incontinence was absent in all 70 patients interviewed.

Some non-motor symptoms occur more frequently in our group and have a pretty big impact on the quality of life of patients with Parkinson's disease (sleep disorders, urinary disorders, bowel disorders, constipation disorders or memory and tendency towards depression). Noteworthy in this study group is that certain symptoms occur even in the early stages of the disease (orthostatic hypotension, impaired memory and concentration), while others in more advanced stages (apathy and lack of interest, depression).

Early identification of non- motor symptoms in patients with Parkinson's disease may improve the management of Parkinson's disease, drawing a complete picture of this disease with pleomorphic manifestations. Some of this symptoms can severely affect the quality of life in these patients and are unresponsive to standard treatment with the known-antiparkinsonian drugs.

Limitations of this study are the small number of patients included and the use of a self-administered questionnaire. A future study is needed to quantify the non-motor symptoms and impact on quality of life of patients with Parkinson's disease.

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