URINARY SYMPTOMS IN PARKINSON’S DISEASE

Prevalence and associated factors

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ABSTRACT - The authors present a cross-sectional study involving 61 patients with idiopathic Parkinson’s disease (PD) who were consecutively examined and compared to a control group with 74 subjects. Only patients who fulfilled the standard diagnostic criteria for PD and whose brain magnetic resonance imaging was normal were included. The objective of the study was to evaluate the prevalence of inferior urinary tract symptoms in PD and to study the possible association between clinical factors to urinary dysfunction. In the patient group, 39.3% presented urinary symptoms when compared to 10.8% in the control group. All symptomatic patients presented irritative symptoms. The most common irritative symptom PD was nocturia, followed by frequency and urinary incontinence. Around 25% of the patients presented functional obstructive symptoms determined by the disease. The most frequent obstructive symptom was incomplete emptying of the bladder. Only the age of the patients and control group were correlated with urinary dysfunction.

KEY WORDS: Parkinson’s disease, urinary symptoms, autonomic symptoms.

The presence of autonomic alterations in Parkinson’s Disease (PD) could influence the diagnosis and prognosis of the disease. In 1817, James Parkinson reported the presence of autonomic signs such as sudoresis, urinary and gastrointestinal symptoms. The lower urinary tract symptoms (LUTS) are classified in irritative and obstructive symptoms. In the irritative group, there are frequency, urgency and nocturia which are caused by hyperactivity of the bladder due to detrusor hyperreflexia. Incomplete emptying, intermittence, weak urinary stream and hesitation are obstructive symptoms. The majority of LUTS found in PD are irritative. Obstructive symptoms or both irritative and obstructive are less frequently found. Detrusor hyperreflexia means a hyperactive bladder due to central nervous system mechanisms. Neurological disorders frequently associated with detrusor hyperreflexia are cerebrovascular disorders, dementia, multiple sclerosis, brain tumor and parkinsonism. According to epidemiological studies of urinary disorders related by Martins Jr. and D’Ancona, 9% of the patients with urinary incontinence had...
The frequency of urinary symptoms in patients with PD revised by Araki and Kuno varied from 37 to 70%3. The distortions in these studies include problems in selecting patients, inclusion of patients with other forms of parkinsonism, the identification of urinary symptoms and the use of medication such as levodopa3,6. Bladder hyperactivity in PD patients can be explained by the removal of inhibitory effects exerted by dopamine neurons, originated in the “pars compacta” of the substantia nigra and mediated by D1 receptors, on the urinary reflex6,7. The presence of Lewy bodies in the autonomic nervous system of patients with advanced PD can explain urinary sphincter dysfunction and rare cases of hyporeflexia of the detrusor muscle3.

LUTS can be measured by using the score scale of the American Urological Association (AUA – 7). This scale is a questionnaire of 7 items which was developed to measure the severity of LUTS among men who have prostate hypertrophy8. It quantifies the urinary symptoms and has correlation with urodynamic findings even in patients without prostate alteration or in females. It can also measure and differentiate the irritative and obstructive symptoms8,9. Patients who have total scores ≥ 8 or irritative scores ≥ 4 and obstructive scores ≥ 5 are considered symptomatic8.

The objective of this study was to analyze the prevalence of LUTS in PD and to study the possible association of sex, age and clinical factors to urinary disorders.

METHOD

The study was comprised of 61 patients selected consecutively from 169 patients with PD who were attended consecutively at the neurological outpatient clinic of Lineu Araujo – SUS Teresina – PI. The control group (74 subjects) was made up of spouses, family and caretakers. Only patients with idiopathic PD who fulfilled the criteria for the established diagnosis were included. Secondary parkinsonism and other types of degenerative parkinsonism were excluded. A brain MRI was done on all participants as exclusion criteria. Patients with dementia, early or severe postural instability, men with prostate hypertrophy or previous prostatectomy and pelvic surgery in women were also excluded. All of the patients were examined after being off levodopa or other dopaminergic medication for 15 hours.

The Unified Parkinson’s Disease Rating Scale (UPDRS) and the Hoehn-Yahr scale were used for neurological evaluation. The urinary symptoms were evaluated by AUA-7 scale, which was applied with assistance of the same examiner (RNCS).

An analytic and observational cross-sectional study was conducted. For descriptive analysis, frequency tables, position and dispersion measurements were used. For the study of association between the variables, the Pearson correlation test was used. The statistic T of Student and the variance analysis (ANOVA) were used to compare the mean scores between the groups. The exact Fisher test was used to study the proportions. The significance level used was 5%.

RESULTS

Sex difference and age - In the patient group 31 (50.8%) were male and 30 (49.2%) female, in the control group 31 (41.9%) were male and 43 (58.1%) female. A significant difference between total (p=0.529) irritative (p=0.94) and obstructive (p=0.053) mean urinary scores for men and women with PD was not observed (Table 1). In Table 2, the mean urinary scores were compared between women with PD and women in the control group and a significant difference between total (p<0.001), obstructive and irritative mean urinary scores was observed. The average age of the group of patients (PD) was 59.6 years. For men, the ages varied from 36 to 77 years with the mean age of 57 and for women the ages varied from 40 to 82 years with mean age of 62 years. In the symptomatic group the ages varied from 40 to 77 years, with mean age of 62.2 years. In the control group the average of age was 59.3 years.

In the PD group a correlation between age and total urinary scores (r=0.351; p=0.0027) and between age and irritative urinary scores (r=0.348; p = 0.0029) was observed. There was no correlation between age and obstructive symptoms (r= 0.197; p= 0.0635). For the control group there was a clear correlation between age and total urinary scores (r= 0.46; p<0.001).

| Table 1. Mean urinary scores (AUA-7) between the groups. |
|----------------------------------------------------------|
| Groups | N | AUA - 7 | |
| | | Total | Irritative | Obstructive |
| PD | 61 | 7.1 | 5.2 | 1.9 |
| Control | 74 | 3.8 | 2.7 | 1.1 |

| Table 2. Mean urinary scores (AUA-7) between women groups. |
|-----------------------------------------------------------|
| Groups | N | AUA - 7 |
| | | Total | Irritative | Obstructive |
| Control | 43 | 3.1 | 2.5 | 0.6 |
| PD | 30 | 6.7 | 5.2 | 1.5 |
Comparing groups - There was a significant difference between total (p<0.0001) irritative (p<0.0001) and obstructive (p<0.0001) mean urinary scores of PD patients and control group. In the group of patients studied, we found 24 patients with total urinary scores ≥ 8, corresponding to 39.3% of the total. All of the symptomatic patients had irritative symptoms and 25% of them also had obstructive symptoms.

In Table 3 there were significant differences between nocturia (p<0.001), diurnal frequency (p<0.001), urgency (p<0.001), and incomplete voiding (p<0.001), when the patients group was compared to the control group.

Duration and severity - The duration of PD varied from 3 months to 20 years, with mean of 4.9 years and median of 3 years. In the symptomatic patients, the duration of disease varied from 1 to 11 years with mean of 4.5 years. No association between the duration of the disease and total (r=-0.004; p=0.48), irritative and obstructive urinary scores was observed.

The severity of PD in the sample studied was measured by using the UPDRS scores. The UPDRS total scores varied from 12 to 98 with mean of 45.8, median of 41 and standard deviation of 22. Among the group of symptomatic patients, the mean total scores was 51.6 while in the non-symptomatic group the mean was 42. No significant difference between the mean total scores (p=0.097) of symptomatic and non-symptomatic PD patients was observed.

with and without urinary symptoms were compared and no significant difference between the mean scores for sector I-mental health, behavior and humor (p=0.73), sector II-daily activities (p=0.86) and sector III- motor functions (p=0.119) was observed. No correlation between the total points of the UPDRS and the total urinary scores (r=0.14; p=0.136) was observed. The possible associations of each cardinal motor symptom with total urinary scores were also studied: tremor (r=0.062; p=0.315); rigidity (r=0.044; p=0.367) and akinesia (r=0.069; p=0.296). No correlation between the motor cardinal symptoms and urinary symptoms was found.

Orthostatic symptoms and postural hypotension - Significant difference between the mean total urinary scores of PD patients with or without orthostatic symptoms (p=0.948) and with or without postural hypotension (p=0.76) was not observed.
Arterial hypertension - Total (p=0.080), irritative (p=0.084) and obstructive (p=0.352) urinary scores between hypertensive and normotensive PD patients were compared and no difference was observed.

Levodopa - There was no significant difference among total (p=0.831), irritative (p=0.473) and obstructive (p=0.377) mean urinary scores of patients who were treated with levodopa and those treated without levodopa.

DISCUSSION

The identification, in the initial phase of parkinsonism, of autonomic symptoms such as urinary symptoms could influence the diagnosis, treatment efficacy and life quality. However, there have been few studies done on the prevalence of LUTS in patients included with established criteria for PD diagnosis from neurological clinics. The majority of the urological studies on PD evaluated patients that had been sent to urological outpatient clinics with LUTS, which biased the selection. The treatment of urinary symptoms in PD patients is sometimes unsuccessful because LUTS could have neurological origin or be a result of drugs such as levodopa or dopaminergic agents and, particularly in men, it could be associated with structural factors like prostate hypertrophy.

When we compared the mean urinary scores between the PD patients and control group the prevalence of urinary dysfunction determined by PD was significant. In this study, the symptomatic patient was 39.3% against 10.8% of non-symptomatic patients. All the symptomatic patient had irritative symptoms and 25% of them also had obstructive symptoms. The prevalence of symptomatic patients in past studies varied from 27% to 75%

Arterial hypertension - There was no significant difference among total (p=0.080), irritative (p=0.084) and obstructive (p=0.352) urinary scores between hypertensive and normotensive PD patients were compared and no difference was observed. To avoid this kind of distortion women, both from PD and control group, were compared and there was significant difference. This reinforces the evidence that urinary dysfunction either irritative or obstructive are related to the disease. Obstructive urinary symptoms could be explained by sphincter and/or somatic pelvic muscle dysfunction. Galloway reported that the bradykinetic external sphincter was responsible for the obstructive symptoms. More recently this opinion was questioned by Myers et al.

In the sample studied the duration of PD was not correlated with its severity, specifically motor symptoms severity. There was no association between duration and urinary symptoms. These facts could be explained by different ages at the onset of the disease according to Diamond et al. By using UPDRS, it was possible to quantify severity and clinical aspects of the disease such as mental state, daily life activity and motor function. Only daily life activity was weakly associated with total urinary symptoms. No difference was observed in the mean total scores of the UPDRS, between symptomatic and non-symptomatic patients suggesting that urinary symptoms were not correlated with severity of the disease. Araki et al. whose studies were based on the Hoehn-Yahr scale and urodynamic methods concluded that urinary function could become progressively worse with PD deterioration.

The possible correlation between the presence of autonomic symptoms and LUTS in the patients with PD was studied. The variables studied were the presence of symptoms when in orthostatic position such as: dizziness, blurred vision, syncope and postural hypotension. The presence of these autonomic symptoms studied separately in PD patients was not correlated to urinary symptoms. The urinary scores of hypertensive and normotensive PD patients were compared, and no significant difference was observed, which agrees with the study of Koskimaki et al.

Differences in the urinary symptomatology between those who used and those who did not use levodopa were not found. The simultaneous use of
two or more drugs such as levodopa, anticholinergic agents and dopaminergic agonistics, could potentially cause LUTS, which limits the possibility of studying the role of each one separately.1,11.

CONCLUSION

Lower urinary tract symptoms were prevalent in 39% of the patients in our study. All the symptomatic patients presented irritative symptoms and 25% also presented functional obstructive symptoms. The most frequent irritative symptoms were nocturia followed by frequency and urinary urgency. The most frequent obstructive symptom was incomplete emptying. Sex, duration and severity of the disease, autonomic symptoms represented by postural hypotension and orthostatic symptoms, the cardinal symptoms (tremor, bradykinesia and rigidity) and levodopa treatment were not associated with urinary symptoms.

REFERENCES

1. Parkinson J. Definition, history and illustrative Cases. In Parkinson J. An essay on the shaking palsy. London: Sherwood Neely, 1817.
2. Chai TC, Steers WD. Neuropsychology of micturition and continence. Urol Clin N Am 1996;23:221–223.
3. Araki I, Kuno S. Assessment of voiding dysfunction in Parkinson’s disease by the International Prostate Symptom Score. J Neurol Neurosurg Psychiatry 2000;68:429–433.
4. Weinberger MW. Differential diagnosis of urinary incontinence. In Ostergard DR, Bent AE. Urogynecology and urodynamic, theory and practice. Baltimore: Williams & Wilkins, 1996:83-89.
5. Martins JR, D’Ancona CA. Disfunção vesical no idoso. In Rodrigues Netto JR, Wroclawski ER. Urologia: fundamentos para o clínico. São Paulo: Ed.Sarvier, 2001:132-135.
6. Singer C, Weiner WJ. Autonomic dysfunction in men with Parkinson disease. Eur Urol 1992;32:134-140.
7. Yoshimura N, Mizuta E, Yoshida O, Kuno S. Therapeutic effects of dopamine D1/D2 receptor agonists on detrusor hiperreflexia in MPTP-lesioned parkinsonian cynomolgus monkeys. T J Pharmacol and Exp Therap. 1998;286:228-233.
8. Barry MJ, Fowler FJ, O’leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. Urol 1992;148:1549-1557.
9. Rhodes T, Gyrmann JC, Jacobsen SJ, Guess H A, Hanson K, Lieber MM. Does the mode of questionnaire administration affect the reporting of urinary symptoms? Urology 1995;46:341-345.
10. Lemack GE, Dewey RB, Questionnaire-based assessment of bladder dysfunction in patients with mild to moderate Parkinson’s disease. Urology 2000;56:250-254.
11. Sakakibara R, Shinotoh H, Uchiyama T. Questionnaire-based assessment of pelvic organ dysfunction in Parkinson’s disease. Auton Neurosci 2001;92:76-85.
12. Pavlakis AJ, Strony MB, Goldstein I, Krane R. Neurourolologic findings in Parkinson’s disease. J Urol 1983;192:80-83.
13. Gray R, Stern G, Malone Lee J. Lower urinary tract dysfunction in Parkinson’s disease: changes related to age and not disease. Age and Ageing 1995;24:499-504.
14. Galloway NT. Urethral sphincter abnormalities in parkinsonism. Br J Urol 1983;55:691-693.
15. Myers DL, Arya LA, Friedman JH. Is urinary incontinence different in women with Parkinson’s disease? Int Urogynecol 1999;10:188-191.
16. Diamond SG, Markham CH, Hoehn MM, Mc Dowell SH, Muentter MB. Effect of age at onset on progression and mortality in PD. Neurology 1989;39:1187-1190.
17. Koskimaki J, Hakama M, Huthala H, Tammela TL. Association of neurologic diseases with lower urinary tract symptoms. Scand J Urol Nephrol 2001;35:377-381.