Idiopathic parkinson's disease

Introduction:

Idiopathic Parkinson’s disease (IPD) is a movement disorder associated with loss of dopaminergic neurons in the substantia nigra and the development of Lewy bodies. A reduction in normal striatal dopamine levels of 80% or more results in the cardinal symptoms of IPD, namely bradykinesia, rigidity, rest tremors and postural instability (1). Although the motor symptoms of Parkinson’s disease are well defined, the non-motor features of this disorder are under-recognized and, consequently, undertreated. Non-motor symptoms and their management have been recognised by the UK National Institute for Clinical Excellence as an important unmet need in IPD (2). Results from a recent international survey show that up to 62% of non-motor symptoms of IPD, such as apathy, pain, sexual difficulties, bowel, urinary incontinence, and sleep disorders might remain undeclared to health-care professionals because patients are either embarrassed or unaware that the symptoms are linked to IPD (3).

Results from early studies suggested that urinary dysfunction (UD) affects between 37% and 70% of individuals with IPD (4). However, many of these studies may have overestimated the prevalence of UD since they were published prior to the recognition of multiple system atrophy (MSA) as a separate disease entity. In addition, many studies recruited patients with symptomatic bladder dysfunction from tertiary referral centers. The use of non-validated questionnaires and the inclusion of patients with other forms of Parkinsonism such as cerebrovascular Parkinsonism may have led to further bias (5). More recent studies, using accepted diagnostic criteria for IPD, have found the prevalence of UD to be between 27% and 39%. When

compared to a control group the relative risk of bladder symptoms in IPD is 2-fold (6).

The aim of this work is to evaluate the urinary symptoms at different stages of IPD severity and its relation to urodynamic tests.

Patients and methods:

This study was conducted on 57 patients with probable IPD attending Urology and Neurology departments, Tanta University Hospital for evaluations of the lower urinary tract symptoms. ALL patients were subjected to, history taking including International Prostate Symptom Score (IPSS), physical examination and neurological examinations. IPD patients were stratified into 5 stages according to Hoehn & Yahr disability stages (7). The IPSS questionnaire was administrated to each patient by one of us to help the patient understand the questionnaire. All men underwent digital rectal examinations and pelvic ultrasonography to exclude prostatic hyperplasia. Eight patients diagnosed with prostatic hyperplasia were excluded from the study. All patients (49 patients) were subjected to urodynamic studies.

Statistical analysis:

Data are presented as mean ± SD. Analysis was performed with SPSS statistical package version 12 (SPSS, USA). For statistical purpose the disease severity stages were divided into mild (stages 1 and 2 H&Y), moderate (stage 3 H&Y) and severe (stages 4 and 5 H&Y).

Results:

Demographic and clinical characteristics of the patients;

This study was carried on 49 patients with probable IPD, 31 male patients and 18 female patients, their age ranged from 56-73 years (mean 63. 73±7. 21 years). The duration of illness was 4-11 years (mean 7. 81±3. 27 years). According to Hoehn and Yaher classification of Parkinson’s disease disability stage, we had 4, 10, 29, 5, 1 patients distributed into stages 1 to 5 respectively. The number of patients in stage 3 was higher than other stages; this may be due to few lower urinary symptoms in early stage of the disease and severe motor and psychiatric symptoms that affect daily life activities in advanced stages. Antiparkinsonian drugs received by the patients were levodopa (41patients), dopamine agonists (39 patients) and anticholinergics (24 patients).

Lower urinary tract symptoms;

The most frequent symptoms of lower urinary tract dysfunctions were symptoms due to storage disorder which include nocturia (77. 5%), urgency (36. 7%) and frequency (32. 6%) (Table 1).

The IPSS index scores;

The total IPSS scores and irritative index scores were correlated significantly with disease severity while obstructive index scores did not (Table 2). Also, there was significant correlation between total IPSS score and quality of life score (Table 3).

Urodynamic parameters;

In this study, we found 33 (67. 3%) patients with detrusor hyperreflexia, 6 (12. 2%) patients with hyporeflexia, 10 (20. 4%) patients with normal detrusor function (Table 4). Volume at initial desire to void and maximum bladder capacity (urodynamic parameters associated with filling phase) were correlated with disease severity while detrusor pressure and post-void residual urine(urodynamic parameters associated with voiding phase) did not (Table 5). There was significant correlation between irritative symptoms score index and volume at initial desire to void and maximum bladder capacity meanwhile the obstructive symptoms score index had no significant relations with any of urodynamic parameters (Table 6).

Antiparkinsonian drugs;

The patients were divided into 2 groups, one group was taking anticholinergic drugs (24 patients) plus Levodopa or dopamine agonists, the second group was taking Levodopa and dopamine agonists(25 patients). There was no significant difference between the 2 groups as regard the mean of urodynamic parameters (Table 7).

Table 1. Frequency of the of lower urinary tract symptoms of IPD patients

Symptoms	Patients	
	NO	%
Nocturia	38	77. 5
Urgency	18	36.

		7
Frequency	16	32.6
Incomplete emptying	4	8. 1
Intermittency	3	6. 1
Weak stream	1	2

Table 2. Total, irritative, and obstructive symptom indexes of IPSS at each stage of disease severity

Stages of disease severity	No Pts	Mean IPSS±SD		
		Irritative	obstructive	total
Mild(stages 1, 2)	14	6. 3±2. 1	1. 4±1. 2	7. 6±2. 4
Moderate(stage 3)	29	7. 9±3. 2	3. 3±2. 6	11. 2±4. 5
Severe(stages 4, 5)	6	10. 4±2. 7	6. 2±3. 5	16. 6±5.

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One-way ANOVA P = 0. 001

Table 3. Correlation between IPSS and Quality of life scores at different stages of disease severity

Stages of disease severity	Total I-PSS mean± SD	Quality of life score mean±SD
Mild (stages 1, 2)	7. 6±2. 4	2. 8±1. 9
Moderate (stage 3)	11. 2±4. 5	3. 7±1. 4
Severe (stages 4, 5)	16. 6±5. 1	5. 2±1. 1

One-way ANOVA P= 0. 003

Table 4. The frequency of urodynamic findings in IPD patients

Stages of H&Y	No. Pts	Normal	Hyperreflexia	Hyporeflexia
1	4	3	1	0

2	10	3	7	0
3	29	4	20	5
4	5	0	4	1
5	1	0	1	0
Total No. (%)	49	10(20. 4)	33(67. 3)	6(12. 2)

Table 5. Urodynamic parameters at different stages of severity of IPD

Stages of disease severity	Volume at initial desire to void (mean±SD) (ml.)	Maximum bladder capacity (mean±SD)(ml.)	Maximum void phase. detrusor pressure (mean±SD)(cm. water)	Post-void residual urine volume. (mean±SD) (ml.)
Mild	115± 28	195± 60	55± 15	13± 12

(14Pts)

Moderate (29Pts)	95± 25	191± 59	57± 20	20± 18
Severe (6Pts)	89± 20	184± 56	59± 25	22±20

One-way ANOVA P= 0. 006

Table 6. Correlation between urodynamic parameters and IPSS scores

Urodynamic parameters	Irritative score		Obstructive score	
	R	P	r	P
Initial void desire vol.	0. 95	0. 001	0. 92	0. 35
Max Bladder capacity	0. 76	0. 04	0. 68	0. 27
Detruser pressure	0. 96	0. 24	0. 89	0. 17
Post residual Urine Vol.	0. 89	0. 43	0. 94	0. 06

Table 7. Correlation between urodynamic parameters (storage phase parameters) and antiparkisonian drugs

Urodynamic parameters	Anticholinergic drug group N0= 24	Non anticholinergic drug group No= 25	P
Initial void desire vol.	102±27	97±25	≥ 0.05
Max Bladder capacity	192±58	188±56	≥ 0.05

Discussion:

Urinary dysfunction in IPD is most frequently caused byurinary storage problems, rather than voiding dysfunction, and manifest as an overactive bladder (8). In the current study, the most prevailing urinary symptom in IPD, was nocturia (up to 77. 5%), followed by urgency (36. 7%) and frequency (32. 6%) and these results are going with previous studies (9, 10). These may lead to urinary incontinence, which may be in part functional if immobility or poor manual dexterity complicates the situation. Since many

patients with IPD have a disturbed sleep pattern and nocturnal polyuria, the actual prevalence of definite nocturia may be overestimated (12).

In this study, the most striking finding of bladder dysfunction in IPD patients is detrusor hyperreflexia, which is reported in 67. 3% of symptomatic patients whereas detrusor hyporeflexia is reported in 12. 2% of IPD patients and normal bladder function in 20. 4%. Another study which evaluated voiding function in IPD found that 67% had detrusor hyperreflexia, 16% had hyporeflexia, 9% had detrusor hypereflexia with impaired contractile function, 3% had hyperreflexia with detrusor-sphincter dyssynergia and only 6% had normal detrusor functions (11). Dopaminergic mechanisms are thought to play a central role in normal micturition control and dysfunction of these may lead to detrusor overactivity. Dopaminergic neurons have both inhibitory and stimulatory effects on micturition acting via D1 and D2 receptors respectively. Such neurons are of particular abundance in the substantia nigra pars compacta (SNC) and the ventral tegmental area (VTA) of the midbrain. The most widely accepted theory is that the basal ganglia inhibits the micturition reflex in the ‘ normal’ situation via D1 receptors, and that cell depletion in the SNC in IPD, results in loss of this D1-mediated inhibition and consequently detrusor overactivity (12). However, 12. 2% of our patients had hyporeflexia which may be explained possibly by drugs especially anticholinergic and dopammiergic drugs which can inhibit bladder function and impairment of autonomic nervous system in advanced IPD.

In this study, both pathological urodynamic parameters, volume at initial desire to void and maximum bladder capacity decreased with disease severity. These findings can be explained by detrusor hyperactivity. In

contrast, other studies showed that post-void residual urine volume increased with disease severity (13, 14). This finding was not fully understood, but this was explained on the assumption that with advanced disease process, long standing hyperreflexia may eventually lead to impairment of bladder contractility together with the hypokinesia of pelvic floor muscles resulting in bladder outlet obstruction with consequent increase in post-void residual urine volume (13, 14). Others believe that they may be secondary to anticholinergics, obstructive uropathy, or point to the presence of multiple system atrophy (15).

Because many IPD patients are on multiple drug therapy, which can inhibit bladder function, the current study, demonstrated that the mean of urodynamic parameters did not differ in patients who did or did not receive anticholinergics or dopaminergic drugs, which suggests that it is part of the IPD itself. These results are going with that of Araki et al. (11), who found no difference in the mean of urodynamic parameters among patients on different antiparkinsonian drugs (11). On the other hand, many studies showed conflicting results(16-18)that some suggest cortical dysfunction (18) or a possible implication of nondopaminergic lesions in the occurrence of bladder dysfunction in IPD (16).

Lower urinary tract symptoms quantified by IPSS showed that irritative symptoms index score correlated with disease severity and with detrusor overactivity that was manifested urodynamically by decrease in volume at initial desire to void and maximum bladder capacity(storage phase) whereas the obstructive symptoms index score did not correlate with disease severity nor urodynamic parameters. In contrast, some other studies show that,

irritative symptoms index score correlated with detrusor overactivity and obstructive symptoms index score correlated with voiding underactivity. Additionally, both irritative and obstructive symptom index scores increased with disease severity (13, 21). This discrepancy between the present study and other studies may be explained by fewer numbers of patients in advanced disease stage and the patients evaluated under multiple drugs therapy in advanced disease.

In conclusion, most of the patients with IPD suffer from urological disorder; most commonly is detrusor hyperactivity which results in irritative urinary symptoms that correlate well with disease severity. These disabling symptoms significantly affect quality of life of IPD patients.

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