Original Article

Urinary Symptoms in Patients with Parkinson's Disease and Progressive Supranuclear Palsy: Urodynamic Findings and Management of Bladder Dysfunction

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Abstract

Objective: The objective of this study is to observe urinary symptoms in patients with Parkinson's disease (PD) and progressive supranuclear palsy (PSP) and advice bladder dysfunction management based on urodynamic study (UDS) findings. **Patients and Methods:** Twenty-two patients (12 males) with PD and PSP (15 and 7, respectively) with urinary symptoms were included in this study. All patients except one were on levodopa and carbidopa medication. UDS was performed, and bladder management determined. **Results:** Mean age was 60.4 years (range 41–73 years, standard deviation [SD] 8.4). Mean illness duration was 31.9 months (range 9–146 months, SD 31.0) and mean duration of urinary symptoms was 14.8 months (range 1–61 months, SD 15.8). Eighteen patients reported nocturia and 16 patients had urgency with or without urge incontinence. Three patients had retention and straining to void and 3 had mixed urinary complaints. Twelve out of 22 patients had absence of voluntary anal contraction on per-rectal examination. UDS was suggestive of 12 patients with neurogenic detrusor overactivity with or without sphincter dyssynergy. Six patients had normal detrusor pressure, and four patients were found to have contractile detrusor. Ten patients had significant postvoid residual. Bladder management included pharmacotherapy, supportive, and behavioral management as appropriate. **Conclusions:** Patients with PD/PSP are known to develop urinary symptoms during illness. Clinical complaints and UDS findings do not necessarily match. UDS is required to manage urinary symptoms. Most of the patients respond to oral antimuscarinic medications along with behavioral and supportive therapy.

Keywords: Parkinson's disease, progressive supranuclear palsy, urinary symptoms, urodynamic study

Introduction

Parkinson's disease (PD) has typically been considered to be a motor neurodegenerative disorder secondary to basal ganglia dysfunction.[1-3] It is characteristically diagnosed with the clinical hallmarks of motor parkinsonism, bradykinesia/akinesia, rigidity, tremor, and postural instability, caused by significant synucleinopathy-induced, nigral degeneration-derived dopaminergic striatal denervation. In the past two decades or so, however, it has become more and more accepted that in PD, a variety of intrinsic nonmotor signs and symptoms accompany motor Parkinsonism. These include autonomic (including bladder, bowel, and sexual dysfunction), sleep, sensory, and neuropsychiatric disturbances.[4,5] These symptoms may arise in early or later stages of the disease in a considerable number of patients and may not be responsive to levodopa. The nonmotor symptoms closely correlate with the progression of extranigral Lewy body and synucleinopathic pathology in PD.[6-8]

PD patients frequently present with lower urinary tract symptoms, often typical of overactive bladder and associated with the urodynamic finding of neurogenic detrusor overactivity (NDO).[9,10] As the neurogenic bladder dysfunction can lead to severe damage of the upper and lower urinary tract, this condition needs early diagnosis and treatment. Hence, there is a need to evaluate the patients based on urinary symptoms at the earliest. The prevalence of urinary symptoms is reported to range between 29% and 73% in various studies, which correlate with the severity of the disease and have an adverse impact on quality of life.[9,11] Patients present with both storage and voiding types of lower urinary tract symptoms-LUTS with former being more common.[12]

Progressive supranuclear palsy (PSP) is a common atypical neurodegenerative parkinsonian disorder, which is a sporadic disease with onset in fifth to seventh decade of life more commonly and first described as a distinct clinicopathological entity by Steele, Richardson, and Olszewski in the early

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1960s.[13-16] A proportion of patients with PSP is known to develop urinary complaints, which might be mild or late onset and adversely affect the quality of life, health economics, and require early institutionalization.[17] Urgency, urge incontinence, high volumes of residual urine are the micturitional disturbances found in PSP. Yamamoto *et al*. observed that urinary storage dysfunction in patients with PSP is not different from PD or multiple system atrophy (MSA), but voiding dysfunction is milder than in patients with MSA and more severe than in patients with PD.[18]

The objective of this study was to report the urodynamic profile of patients with PD and PSP with neurogenic bladder dysfunction based on urodynamic study (UDS) findings. We also wanted to observe the correlation between clinical symptoms and neurogenic bladder pattern in patients with urinary symptoms in PD and PSP. The bladder management strategy was based also on the UDS findings.

Patients and Methods

This prospective, cross-sectional study was conducted in the Department of neurological rehabilitation of a quaternary hospital-based research institute. It was part of a nonfunded project for a period of 2 years (October 2015–September 2017). The local ethics committee approval was obtained for the project, and informed consent was taken from all the patients before enrolling them for the study. Patients diagnosed with PD and PSP with urinary complaints were included in this study. Patients of all ages and both sex included irrespective of the duration of illness and type of urinary complaints. Patients with MSA, patients with parkinsonian disorders such as traumatic, drug-induced, and vascular PD were excluded from the study.

Patient selection

Patients with PD (diagnosed according to 'the UK PD society brain bank clinical diagnostic criteria' by the neurologist) and PSP (diagnosed according to "The National Institute for Neurological Disorders and Stroke-Society for PSP criteria" for the diagnosis of clinically probable PSP by the neurologist) with urinary symptoms were recruited in the study. During the study, a total of 483 patients with PD and PSP were referred from the Department of Neurology to our department for rehabilitation (predominantly balance, gait, and activity of daily living training-related issues). During the same period, 48 patients with PD and PSP, who were having urinary complaints, were referred for UDS and bladder dysfunction management. Sixteen patients seen in outpatient services in both the departments expressed desire to get further investigated (including UDS) from their native places. The remaining 32 patients were assessed in detail including further investigations. After initial clinical assessment, they were advised to report back with 3 days bladder (voiding) diary and abdominal (kidneys, ureters, and bladder [KUB]) ultrasound report (to observe prostate status in male patients and to observe postvoid residual (PVR) urine in bladder and backpressure changes in the ureter and kidney). In 10 patients, UDS could not be done on the scheduled appointment and date because of some reasons (most common being the inadequate bowel preparation) and eventually patients were lost. Hence, the study included 22 patients of PD and PSP with urinary symptoms, who did undergo UDS.

Patients' sociodemographic profile was noted. Their illness duration and severity of impairment and disability were assessed using appropriate scales. Urinary complaints and duration were noted. Medical comorbidities and the medications they were put on for these illnesses as well as for PD and PSP were also noted.

Urodynamics

Filling and voiding cystometry was carried out using multichannel pressure recording technology with Life-Tech Urolab Primus (USA) system. Patients were given a bowel program on previous day and enema on the morning of procedure for bowel evacuation. All the bladder sensations were defined according to the International Continence Society-guidelines and terminology and comprehensibly explained before the study.[19] Filling cystometry was performed with the patients in the supine position on the urodynamic table. Bladder filling was done with normal saline at rate of 10 ml/min with two-lumen 6 Fr catheter in urethra. Patients were made to sit during voiding phase to void urine. Recordings were made during the filling and voiding phase. Sphincter electromyography was performed to observe sphincter activity and possible synergic/detrusor sphincter dyssynergia (DSD) pattern. It was done using anal patch surface electrodes. The complete data were captured, and analysis of graph and values of relevant pressures was done.[20,21] The final urodynamic diagnosis was made, and management determined and instituted consisting of pharmacotherapy, supportive and behavioral measures.

Data analysis

Data were analyzed using Statistical package for social science SPSS version 17.0 (IBM, IL, Chicago, USA). Descriptive statistics included frequency, mean, and standard deviation for quantitative variables such as age, duration of illness, duration of urinary complaints, and illness severity scores. It also included detrusor characteristics and management advised.

Results

Patient profile

Fifteen patients had PD and 7 were diagnosed to have PSP. Gender distribution was almost equal with 12 males and 10 females in the study. Their age ranged from 41 to 73 years (mean 60.4 years, standard deviation [SD] 8.4). Unified PD Rating Scale-UPDRS was used to assess the severity of illness in patients with PD.[22] Scores ranged from 15 to 48 with a mean score of 19.9 (SD 17.9) suggesting that the patients were either early PD patients or "good responders" to dopaminergic medications. Similarly, PSP rating scale was used for patients

with PSP (0–100). The score ranged from 9 to 56 with a mean score of 18.6 and SD 11.9. The duration of illness varied from 9 to 146 months with a mean of 31.9 months and SD 31.0. The duration of urinary symptoms varied from 1 to 61 months with a mean of 14.8 months and SD15.8. Twenty-one patients were taking dopaminergic medication (combination of levodopa and carbidopa) at the time of assessment and procedure in rehabilitation. About the medical comorbidities; five patients had hypertension, three had type-2 diabetes mellitus, one patient was on antidepressants, and nine patients were diagnosed with dementia. All were taking medications as per the advice of physician/neurophysician.

Urinary complaints and Abdominal (kidneys, ureters, bladder) Ultrasound

Eighteen patients had a complaint of nocturia, (increased night time frequency), which was found to be the most common urinary complaint. This was followed by the complaints of urgency with or without urge incontinence, which was noted in 16 patients. Three patients had obstructive urinary complaints in the form of hesitancy and straining to void and retention. Three patients had mixed urinary complaints.

Ultrasound (KUB) was suggestive of significant PVR in three patients. No patient was reported to be showing back pressure changes in the form of hydroureter or hydronephrosis. Out of 12 males, 1 patient was observed to be having prostate enlargement.

Urodynamic findings

Per rectal/anal examination is routinely performed in all patients before commencing saline cystometrography. The examination suggested that 20 patients had anal reflex present whereas it was absent in the other two. Voluntary anal contraction (VAC) was present in only 10 patients and absent in the remaining 12.

During filling cystometrography, 14 patients were found to have normal cystometric capacity. Their urodynamic findings are mentioned in Table 1.

During voiding10 patients were found to have significant PVR. This was remarkably different to what was observed with ultrasound, which suggested only three patients to be having significant PVR. Twelve patients had nil/insignificant PVR.

Based on UDS findings (especially detrusor characteristics), eight patients were advised antimuscarinic medications (tolterodine-6, and oxybutynin-2), ten patients were advised timed voiding, and eight patients were put on clean intermittent self-catheterization, with or without anti-muscarinic. Four patients were advised voluntary micturition without supportive therapy.

Table 1: Bladder characteristics in patients with Parkinson's disease and progressive supranuclear palsy based on urodynamic findings

Clinical diagnosis	Number of patients				
	Normal detrusor	Acontractile/ hypo contractile detrusor	NDO with sphincter synergy	NDO with DSD	Total
PD	2	4	4	5	15
PSP	4	0	2	1	7
Total	6	4	6	6	22

NDO=Neurogenic detrusor overactivity, DSD=Detrusor sphincter dyssynergia, PD=Parkinson's disease, PSP=Progressive supranuclear palsy

Discussion

PD patients are known to develop LUTS following motor disorder. There are reports suggesting direct correlation between dopaminergic denervation and LUTS, which effectively means onset or worsening of urinary complaints with worsening of motor disorder.[5,23]

Storage symptoms have been known to be more common with nocturia or night time frequency reported to be the most common complaint in patients with PD.[18] Hesitancy with straining to void is reported to be the most common voiding complaint in some studies.[5,24,25] In the present study, we also observed nocturia, urgency, and urge incontinence to be the most common complaints (72.7%), but only three patients had complaints of straining to void, and the remaining three patients had mixed urinary symptoms. Hence, voiding complaints were less commonly observed in our pool of patients, which is difficult to explain with the small sample size.

Constipation has been reported to be present in more than half of the patients with PD with one-fifth reporting fecal incontinence.[5,26] Although we did neither record bowel-related complaints in patients nor was the objective of the study to advise bowel management; however, it is interesting to note that 12 out of 22 patients had absent "voluntary anal contraction-VAC" with the majority (20/22) had anal reflex and tone present. The absence of VAC is of significance as it may lead to the episodes of bowel incontinence in these patients and while giving "bowel program", one has to be mindful of it.

It has been reported that in levodopa naïve mild PD patients, initially the dose causes deterioration of urinary dysfunction; however, with chronic use, the urinary symptoms tend to improve.[27] In the present study, all patients except 1 was taking levodopa plus carbidopa at the time of reporting to us as well as during the time UDS was performed and the dosage was not altered. Hence, the effect of this particular medication on urinary complaints and UDS observation is impossible to comment on in the present study.

In PD, degeneration of basal ganglia results in partial or total disconnection of the micturition reflex from the voluntary control resulting in uninhibited detrusor contractions at low bladder volumes. This is mediated through D1 receptors. Cell depletion in the substantia nigra results in loss of this inhibition resulting in detrusor overactivity.[28,29] Similarly, frontal lobe dysfunction with tau protein accumulation and

neuropathological changes in the substantia nigra, striatum, medial globus pallidus, subthalamic nucleus, and several brainstem nuclei are responsible for urinary dysfunction in patients with PSP.[30,31]

Studies in the past have suggested that the majority of the patients with PD were found to have overactive detrusor with detrusor-sphincter synergy based on UDS.[32,33] Our study showed that mixed results with almost equal number of patients with overactive detrusor had synergic and dyssynergic sphincter. However, with a small sample size in our study, it will not be appropriate to draw conclusions or corroborate or refute the findings of earlier studies. The important observation was that more than half of the patients were found to have overactive detrusor in the present study. Six out of 22 patients (27.3%) were found to have normal detrusor pressure, meaning thereby that they showed no/minimal detrusor activity during filling phase and were able to generate normal pressure during voiding phase. Two-third of these patients had PSP as diagnosis whereas the remaining two were cases of PD. Four of these patients were advised voluntary micturition without medication, supportive, or behavioral measures. The remaining two had nonrelaxing sphincter and were advised timed voiding with clean intermittent self-catheterization (CISC) for bladder emptying. Intact sensations make it painful for them to perform timed voiding with CISC as compared to patients with myelopathy with sensory loss or impairment. Most of the patients, who reported in the follow-up showed good compliance with the management advised. Eight patients, found to have NDO, were advised with antimuscarinic medications in the form of either tolterodine or oxybutynin. Most of the patients responded well with a combination of oral anticholinergic (antimuscarinic) medication along with behavioral and supportive management.

Although anticholinergic medications are the first-choice drugs for the management of NDO, one must balance the therapeutic benefits with potential adverse effects. These medications are known to cross blood–brain barrier and adversely affect cognition/patients with dementia.[34,35] One important observation in the study was as many as nine patients were already diagnosed as having dementia (6 patients with PSP and 3 with PD). The role of anticholinergic medications has to be carefully observed in these patients. A newer medication Mirabegron, which is a beta-3 adrenergic agonist and causes suppression of the detrusor contractility, has to be tried especially in patients already having dementia associated with PD/PSP. We have no experience with this medication due to nonavailability locally.

Patients with nonrelaxing sphincters or DSD were advised medications such as Duloxetine (Selective serotonin-norepinephrine reuptake inhibitor-SNRI) or imipramine (Tricyclic Antidepressant) with varying doses and results. We have limited experience with these medications in patients with PD and PSP but have used them extensively in myelopathy patients with mixed results.

Other than oral antimuscarinic medications, there are some other management options such as local botulinum toxin A injections or deep brain stimulation (DBS) especially in patients with advanced PD.[36,37] DBS has been reported to influence NDO also and in turn helps in management of urinary symptoms.

Conclusions

Patients with PD and PSP are known to develop urinary symptoms during illness. Clinical complaints and UDS findings do not necessarily match in patients. UDS is recommended to manage these symptoms. Most of the patients respond to oral antimuscarinic medications along with behavioral and supportive therapy. As these patients, especially those with PSP, are known to develop cognitive decline/dementia during illness, the patients need to be followed up regularly to observe deterioration. Some patients may require other methods of bladder management such as botulinum toxin injections and DBS, etc.

The study has some limitations such as small sample size, which is mainly because of patients' reluctance to get short-term admission in neurological rehabilitation department for detailed work-up and UDS.

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Conflicts of interest

There are no conflicts of interest.

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