

NEUROLOGY

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Neurology 2008;70:299

DOI 10.1212/01.wnl.0000296826.61499.26

This information is current as of February 15, 2011

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Lower urinary tract symptoms in dementia with Lewy bodies, Parkinson disease, and Alzheimer disease



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ABSTRACT

Objective: The present study sought to investigate lower urinary tract symptoms and urodynamic and cystometric findings in Parkinson disease (PD), dementia with Lewy bodies (DLB), and Alzheimer disease (AD).

Methods: Included were patients with frequency, urgency, incontinence, and nocturia, without major bladder outflow obstruction. The protocol comprised physical examination, urine analysis, prostate specific antigen, 24-hours frequency of micturition, mean voided volume (MVV), free flow before instrumentation ($Q_{\max_{\text{before}}}$), post-void residual volume (PVR), and cystometry.

Results: Fifteen patients with DLB and PD and 16 patients with AD were examined. MVV, PVR, $Q_{\max_{\text{before}}}$ and with transurethral catheter, cystometric bladder capacity, and detrusor pressor at maximum flow were similar in the three groups and corresponded to values of the general elderly population. Urge episodes and urge incontinence were observed in 93 and 53% of the patients with DLB, 53 and 27% of the patients with PD, and 19 and 12% of the patients with AD, and detrusor overactivity in 92% of the patients with DLB, 46% of the patients with PD, and 40% of the patients with AD.

Conclusions: Urgency and urge incontinence suggest detrusor overactivity, which was more prevalent in dementia with Lewy bodies than in Parkinson disease and Alzheimer disease, whereas mean voided volume, free flow, cystometric bladder capacity, and detrusor pressor were similar in the groups. Frequency of micturition could not be reliably assessed in patients with dementia.

Neurology® 2008;70:299-303

GLOSSARY

AChe-I = acetylcholinesterase inhibitor; **AD** = Alzheimer disease; **aNL** = atypical neuroleptics; **DA** = dopamine agonist; **DLB** = dementia with Lewy bodies; **EMG** = electromyography; **ICS** = International Continence Society degree of infravesical obstruction; **KW ANOVA** = Kruskal-Wallis analysis of variance; **LD** = levodopa; **LUTS** = lower urinary tract symptoms; **MF** = mean frequency of micturition; **MMSE** = Mini-Mental State Examination; **MSA** = multiple system atrophy; **MVV** = mean voided volume; **MW-U** = Mann-Whitney *U* test; **PD** = Parkinson disease; **PVR** = post-void residual volume.

The prevalence of lower urinary tract symptoms (LUTS; frequency, urgency, and urge incontinence) in Parkinson disease (PD) correlates with age, dementia, and duration and progression of motor symptoms.¹⁻³ In dementia with Lewy bodies (DLB),⁴ which is clinically characterized by progressive dementia, fluctuations in cognitive functions, and psychosis developing before, at the same time as, or shortly after the onset of parkinsonian motor symptoms, urinary incontinence is an early symptom, whereas in Alzheimer disease (AD) it occurs in an advanced stage of the disease.³ The present study sought to investigate whether LUTS and urodynamic and cystometric findings differ in PD, DLB, and AD.

METHODS Included were consecutive patients with PD without dementia, with probable DLB,⁴ and with probable AD.⁵ Enrolled patients had a negative history of TIA or stroke and except for cortical or subcortical atrophy cranial CT or MRI was normal. Neurologic examination did not reveal cerebellar signs, pyramidal signs, or supranuclear palsy suggestive of multiple system atrophy (MSA) or progressive supranuclear palsy.^{6,7} Spinal cord lesions, vertebral stenosis, and disc hernias

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Disclosure: The authors report no conflicts of interest.

Table 1 Demography, clinical data, and therapy (mean ± SD)

	Age, y	M/F*	Parkinson duration, y	Hoehn & Yahr score	ICS score (0-6)	L-Dopa (daily dosage in mg), other therapies	Mini-Mental State Examination	Neuro-urologic history/ no. of patients
DLB (n = 15)	72.7 ± 6.5	11/4	5.2 ± 2.7	4.4 ± 0.9	1.4 ± 1.1	387 ± 246 [†]	20.2 ± 5.2	Urgency and frequency/12; incontinence/8; supposed bladder outflow obstruction/4
PD (n = 15)	67.8 ± 10.5	12/3	10.6 ± 9	3.6 ± 0.7	1.5 ± 0.9	546 ± 345 [‡]	Not done	Urgency and frequency/7; incontinence/5; supposed bladder outflow obstruction/7
AD (n = 16)	74.7 ± 9.2	7/9			1.1 ± 1.3	§	21.5 ± 4.7	Urgency and frequency/12; incontinence/3; supposed bladder outflow obstruction/3
KW ANOVA (p)	0.13				0.53			
MW-U test (p)			0.17	0.02		0.34	0.50	

*No significant differences in male/female ratio between the groups (χ^2 ; $p = 0.08$).

[†]DLB: LD 13, DA 1, AChE-I 4, aNL 2 patients.

[‡]PD: LD 12, DA 7, AChE-I 0, aNL 0 patients.

§AD: LD 1, DA 0, AChE-I 7, aNL 1 patient.

ICS = International Continence Society degree of infravesical obstruction; DLB = dementia with Lewy bodies; PD = Parkinson disease; AD = Alzheimer disease; KW ANOVA = Kruskal-Wallis analysis of variance; MW-U = Mann-Whitney *U* test; LD = levodopa; DA = dopamine agonist; AChE-I = acetylcholinesterase inhibitor; aNL = atypical neuroleptics.

were also clinically ruled out. Infravesical obstruction (according to the International Continence Society) was null, mild, or moderate.⁸ Enrolled patients or their caregivers reported frequency, urgency, incontinence, nocturia, or symptoms suspicious of mild to moderate bladder outflow obstruction (reduced force of stream, hesitancy, incomplete bladder emptying, straining). The patients had not been previously treated with antispasmodic anticholinergic medication.

Patients were informed about the purpose of the examination, which is part of the standard clinical workup protocol for patients with suspected neurogenic bladder disorders at the Neurourology Unit of the Department of Neurology, Innsbruck Medical University. Neuro-urologic investigation comprised a detailed history of LUTS, physical examination (digital rectal examination, pinprick sensation of the sacral dermatomes, bulbocavernous reflex, anal sphincter tone and reflex, voluntary anal sphincter contraction) as well as urine analysis and PSA.

Micturition and voided volumes were recorded for a minimum of 48 hours and the 24-hour frequency of voiding (MF) as well as mean voided volumes (MVV; mL) calculated. Urodynamic investigation, performed before treatment of LUTS, comprised uroflowmetry, recorded as “free flow” before transurethral instrumentation ($Q_{\max_{\text{before}}}$) and determination of post-void residual volume (PVR; mL; bladder scan, Diagnostic Ultrasound Corp). Cystometry and pressure flow studies¹ were performed if impaired detrusor function or bladder outflow obstruction were assumed using a 10 French double lumen urodynamic catheter introduced transurethraly into the bladder, a rectal balloon catheter for simultaneous assessment of intraabdominal pressure, and surface electrodes for random electromyography (EMG) of the pelvic floor musculature (Urodynamic Unit “Ellipse,” Andromeda, Taufkirchen, Germany, AUDACT evaluation program). Cystometric bladder capacity (CBC; volume at maximum desire to void; mL), maximum flow rate (Q_{\max} ; mL/sec), detrusor pressure at maximum flow rate ($P_{\text{detr}_{Q_{\max}}}$; cm H₂O), and EMG activity of the perineal musculature were recorded. Further investigations of autonomic functions, such as sudomotor tests, heart rate analyses, or cardiac

¹²³I-MIBG uptake, as performed elsewhere in DLB and PD were not done.^{9,10} Group comparisons were performed using the Kruskal-Wallis analysis of variance, the χ^2 , and the Mann-Whitney *U* test. Data are indicated as means ± SD.

RESULTS Table 1 summarizes demographic and neurologic findings, degree of infravesical obstruction (range 0 to 6),⁸ Mini-Mental State Examination (MMSE) scores, pharmacotherapy, and urologic history. There were no differences among the three groups with respect to age or the degree of infravesical obstruction. Male/female ratio tended to be different in the three groups (χ^2 $p = 0.08$). Duration of parkinsonian motor symptoms was insignificantly longer in PD than in DLB and the Hoehn and Yahr scores during “practical-off” were higher in DLB than in PD, suggesting faster progression of parkinsonian motor impairment in DLB than in PD. The MMSE scores were comparable in DLB and AD. The mean daily dosage and the proportion of patients on levodopa therapy were similar for DLB and PD (13 of 15, and 12 of 15; χ^2 ; $p = 0.24$). The proportion of patients with DLB and AD treated with an acetylcholinesterase inhibitor (4 of 15, and 7 of 16) was comparable ($p = 0.32$). Significantly more patients with PD than DLB were treated with a dopamine agonist (7 of 15, and 1 of 15; $p = 0.013$). Only two patients with DLB and one with AD received atypical neuroleptics.

Table 2 shows MF, MVV, number, and percentage of patients with episodes of urgency and urge incontinence, $Q_{\max_{\text{before}}}$, and PVR. MF, MVV, $Q_{\max_{\text{before}}}$, and PRV were similar in the

Table 2 Frequency of voiding, mean voided volumes, urge and incontinence, uroflowmetry, and post-void volumes (mean \pm SD)

	MF (in 24 h)	MVV, mL	Urgency episodes, n (%)	Urge incontinence episodes, n (%)	Qmax _{before} , mL/sec	PVR, mL
DLB (n = 15)	7.9 \pm 3.4	198 \pm 79	14 (93)	8 (53)	12.1 \pm 4.7	46 \pm 50
PD (n = 15)	6.4 \pm 1.5	196 \pm 53	8 (53)	4 (27)	13.4 \pm 7.2	45 \pm 72
AD (n = 16)	5.9 \pm 1.6	165 \pm 71	3 (19)	2 (12)	14 \pm 7.5	36 \pm 65
KW ANOVA (p), χ^2 (p)	0.34	0.48	<0.001	0.04	0.79	0.37

MF = mean frequency of voiding; MVV = mean voided volume; Qmax_{before} = maximum free flow before transurethral instrumentation; PVR = post-void residual urine volume; DLB = dementia with Lewy bodies; PD = Parkinson disease; AD = Alzheimer disease; KW ANOVA = Kruskal-Wallis analysis of variance.

three groups. MF, however, could not be reliably assessed in demented incontinent patients needing sanitary pads. Urgency and urge incontinence episodes were more prevalent in DLB than in PD or AD. Table 3 summarizes cystometric findings. CBC, Qmax, and Pdetr_{Qmax} were similar in all groups. Uninhibited detrusor contractions during bladder filling (detrusor overactivity) were found in a larger proportion of patients with DLB than PD or AD. No detrusor-sphincter dyssynergia was observed. The difference in CBC between patients with and without detrusor overactivity was not significant (median 244 and 299 mL; $p = 0.324$; Mann-Whitney U test).

Only in two patients (one AD and one DLB) was detrusor overactivity not associated with a history of urgency. One patient of each group reported urgency but detrusor overactivity was not found. Patients with PD and DLB with detrusor overactivity had significantly higher Hoehn and Yahr scores than did those without detrusor overactivity (Mann-Whitney U test; $p = 0.02$). Prevalence of urgency, urge incontinence, and detrusor overactivity was similar in patients with PD treated with and without dopamine agonists (χ^2 ; $p > 0.29$).

DISCUSSION The three groups were comparable with respect to age and degree of infravesical obstruction. There was a preponderance of male pa-

tients in the DLB and PD groups; however, the male-female ratio was not statistically different in DLB, PD, and AD. Moreover, severity of dementia was comparable in patients with DLB and AD.

PVR, CBC, Pdetr_{Qmax}, and the prevalence of incontinence in our patients with DLB corresponded to recently published findings in patients with DLB.¹¹ PVR, CBC, and the prevalence of detrusor overactivity in our patients with PD and AD were also similar to recent studies in patients with PD and AD.^{1,12,13} PVR, CBC, Qmax, and Pdetr_{Qmax} in our patients were comparable to the findings of a recent study of persons representing the general elderly population¹⁴ suggesting that these parameters are essentially normal.

In demented and incontinent patients MF and voided volumes could not be precisely assessed. This is probably the reason why we did not find significant differences in MF between the groups. Qmax_{before}, Qmax, PVR, and Pdetr_{Qmax} were normal and no differences between PD, DLB, and AD were found. Moreover, CBC was not different in the three groups although a higher prevalence of urgency and urge incontinence was seen in DLB than in PD or AD. CBC correlates with urgency, urge incontinence, and frequency, but varies markedly between individuals.^{1,14} Studies in larger collectives might

Table 3 Cystometric findings (mean \pm SD)

	CBC, mL	Qmax, mL	Pdetr _{Qmax} , cm H ₂ O	Detrusor overactivity, n (%)	Detrusor-sphincter dyssynergia
DLB (n = 12)	254 \pm 185	11.7 \pm 4.7	38.5 \pm 33.7	11 (92)	0
PD (n = 13)	256 \pm 76	15.3 \pm 6.7	42.2 \pm 19.4	6 (46)	0
AD (n = 10)	297 \pm 154	12.3 \pm 6.2	45.8 \pm 21.5	4 (40)	0
KW ANOVA (p), χ^2 (p)	0.97	0.30	0.21	0.02	

CBC = cystometric bladder capacity; Qmax = maximum flow; Pdetr_{Qmax} = detrusor pressure at maximum flow rate; DLB = dementia with Lewy bodies; PD = Parkinson disease; AD = Alzheimer disease; KW ANOVA = Kruskal-Wallis analysis of variance.

reveal smaller CBC in DLB and PD than in AD. Only in two demented patients with detrusor overactivity (one patient with DLB and one patient with AD) was history of urgency negative. In one patient of each group there was a history of urgency; however, detrusor overactivity was not found. Larger studies are needed to assess the positive and negative predictive value of a history of urgency and urge incontinence for neurogenic detrusor overactivity. Nevertheless, simple history of urgency and urge incontinence appears to be a better predictor of detrusor overactivity than micturition protocols.

Detrusor overactivity was found to correlate with the Hoehn and Yahr scores. It is likely that neurodegeneration in the nigrostriatal dopamine system causes disinhibition of the micturition reflex resulting in detrusor overactivity in PD and DLB.^{15,16} Studies in PD have also revealed significant loss of neurons in the intermediolateral cell column which inhibits detrusor muscle function.^{17,18} Moreover, degeneration of neurons in the frontal cortex may disinhibit the pontine bladder control center.¹⁹ Detrusor overactivity in AD might be due to pathologic changes in the substantia nigra and the frontal cortex and also related to concomitant Lewy-type pathology.²⁰⁻²²

The prevalence of urgency and urge incontinence was lower in AD than in DLB. Whether or not LUTS contribute to the differential diagnosis of DLB and AD needs to be verified in larger studies and with autopsy confirmation. At present, urinary incontinence is considered a nonspecific supportive feature of DLB.²² In contrast to MSA, there was no evidence of detrusor-sphincter dys-synergy or sphincter insufficiency in our patients.^{16,23}

Did pharmacotherapy (table 1) influence the results of the study? The effect of levodopa and dopamine agonists on LUTS is complex. Bladder capacity and detrusor overactivity and thus urinary urgency and incontinence may improve or deteriorate in response to dopaminergic treatment.^{2,15} Prevalence and daily dosage of levodopa therapy were similar in patients with DLB and PD. Prevalence of urgency, urge incontinence, and detrusor overactivity was similar in patients with PD treated with and not treated with dopamine agonists and the proportion of patients with AD and DLB taking an acetylcholinesterase inhibitor was similar. Therefore we assume that the group differences were not related to pharmacotherapy.

Received January 23, 2007. Accepted in final form July 2, 2007.

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DOI 10.1212/01.wnl.0000296826.61499.26

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