

Lower Urinary Tract Dysfunctions in Dementia and Parkinson's disease

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Introductions

- **Lower urinary tract dysfunction(LUTD) occurring in patients with cerebral disorder is one of the emerging issue especially in ‘*The Aging Society*’**
- **Understanding why LUTS occur in patients with cerebral disorder and identify the patterns of LUTD in these patients is the first step for establishment of the treatment stargegies.**



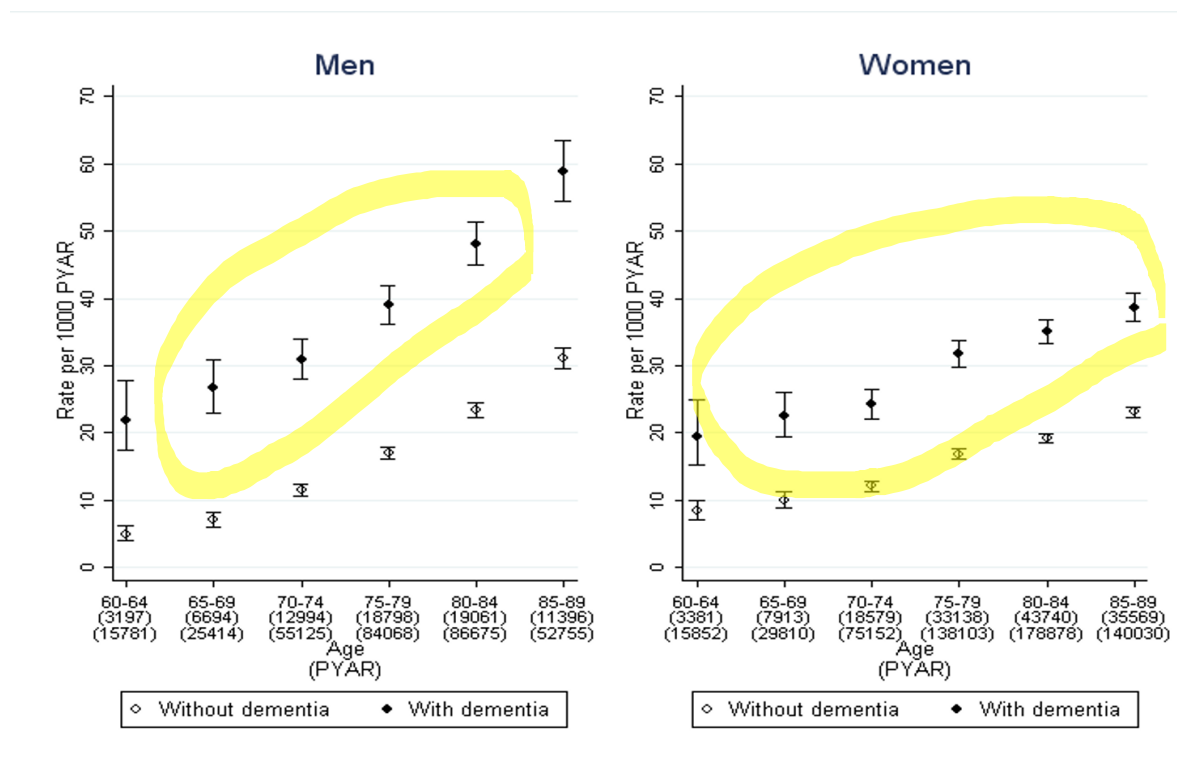
Introductions

- **The most common degenerative neurological disease is Alzheimer's disease and the second common is Parkinson's disease in aging population.**
- **The main objectives in this presentation are:**
 - ✓ *To review the neurological basis for LUT dysfunction following common cerebral disorders such as Parkinson's disease(PD) and the dementias.*
 - ✓ *To explore the spectrum of LUT symptoms in PD and the dementia.*
 - ✓ *To review strategies for management of LUT symptoms in these patients.*



LUT dysfunction in patients with Dementia

- Dementia is a syndrome in which there is deterioration in memory, thinking, behaviour and the ability to perform everyday activities.



Prevalence of Urinary Incontinence in Patients with or without Dementia



LUT dysfunction in patients with Dementia

- Types of dementia – *not all dementia is alzheimer's disease*

TABLE I. Classification of Dementia According to the Etiology

Neurodegenerative diseases	Other causes
Alzheimer disease (ALD) (60%)	Cerebro vascular (20%)
Lewy body disease (LBD) (10%)	Normal pressure hydrocephalus (NPH)
Cortico-basal degeneration	Neoplasia, trauma,
Progressive-focal degeneration	Chronic intoxications
	CNS ^a infections (lues, AIDS ^b)
	Non-infection-associated inflammations
	Pseudodementia in psychiatric diseases
	Other structural defects:
	cerebral hypoxia, radiation

- The occurrence of LUTS are different, therefore the management should be tailored according to the type of dementia.



LUT dysfunction in patients with Dementia

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

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	



LUT dysfunction in patients with Dementia

- **Alzheimer disease (AD)**

- ✓ *Prevalance of UI – 23% - 48%*
- ✓ *Onset of incontinence : late-stage*
- ✓ *Behavioural therapy strategies, including toilet training and prompted voiding, are especially useful*
- ✓ *Antimuscarics may enhance behavioral therapy, especially when the bladder capacity is reduced.*

- **Lewy Bodies Dementia (LBD)**

- ✓ LUTS usually occur **earlier during the course** of the disease
- ✓ DO are more common in LBD than in patients with AD
- ✓ urodynamics are useful for differential diagnosis, and are therefore helpful for the physician



LUT dysfunction in patients with Dementia

▪ **Vascular Demntia (VD)**

- ✓ *Loss of bladder filling sense*
- ✓ *Det underactivity Vs. Det. Overactivity : 45% > 55%*
- ✓ *Mainly dependent to congitive deficit, disorientation and motor ristraction*
- ✓ *Improving motor mobility shound be included in behavioral therapy*

▪ **Normal pressure hydeocephalus (NPH)**

- ✓ *Highly prevalence of LUTS : up to 93%*
- ✓ *Symptoms of NPH may be reversed by shunt surgery (such as ventriculo-peritoneostomy)*
- ✓ *Usally combination medicaitns are recommended.*



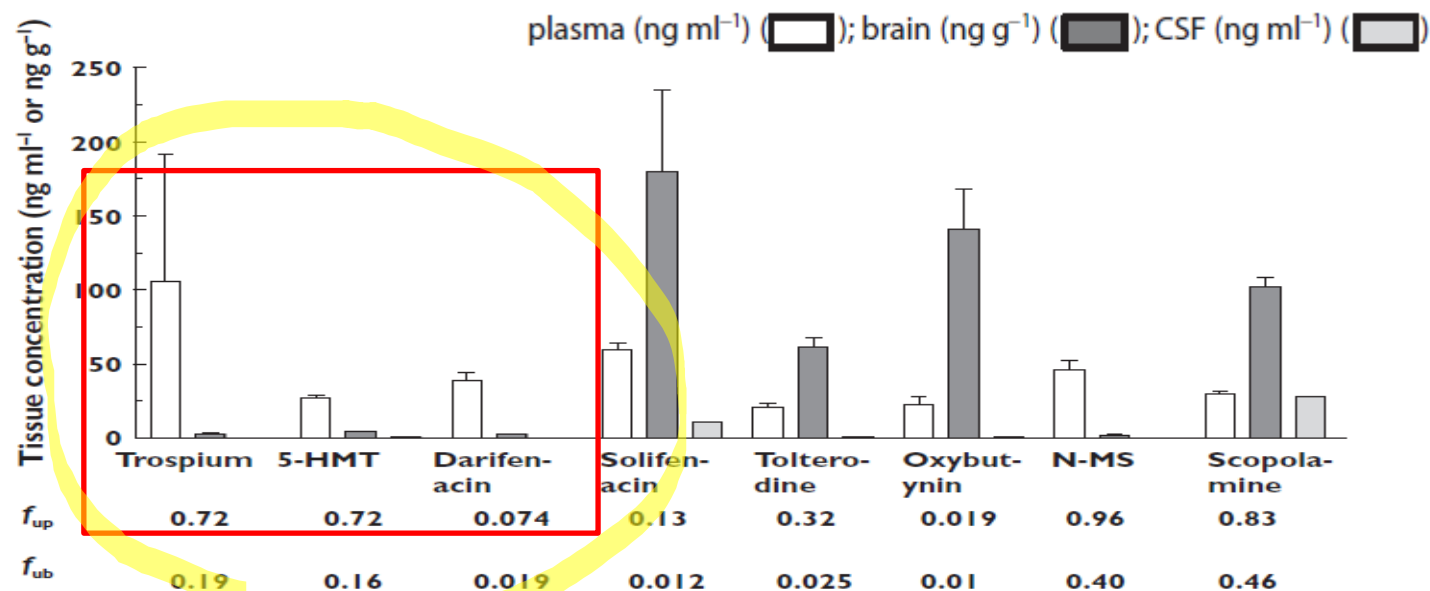
LUT dysfunction in Dementia – pharmacotherapy for dementia

- **Medical treatment for Dementia**
 - ✓ *1st line Tx : cholinesterase inhibitors*
 - ✓ *2nd line Tx : memantine (NMDA-antagonist)*
- **Cholinesterase-Inhibitors are given by the neurologist to increase acetylcholine activity in the brain by stimulation M1 receptors**
- **Cholinesterase-Inhibitors may also be effective in the periphery, thus inducing/increasing urge-incontinence.**



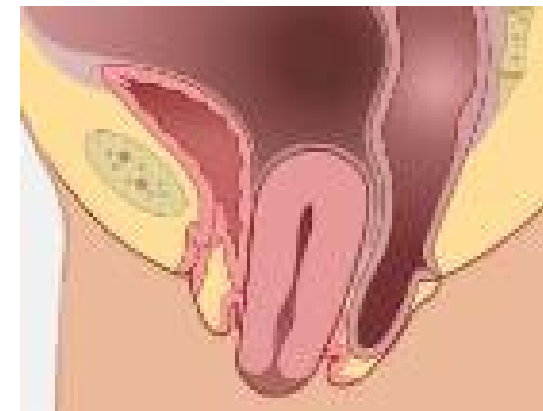
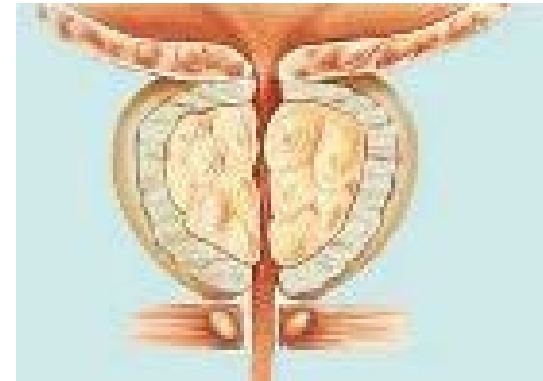
LUT dysfunction in Dementia – Paradox in medication

- Cholinesterase-inhibitors are given by the neurologist to improve memory
- Antimuscarinics are given by the urologist to improve urgency



LUT dysfunction in Dementia – Comorbidity

- LUT problems in patients with dementia are not necessarily related to the neurologic pathology
- Other diseases such as prostate pathology and pelvic organ prolapse might also have an influence
- Clinical assessment including history, clinical examination, urine analysis, bladder diary, free flowmetry and PVR should be as comprehensive as possible



LUT dysfunction in Dementia – Summary

- **Various forms of dementia cause different LUTS at different times during disease process and therefore require individualized treatment strategies.**
- **Despite of the type of dementia, the treatment of LUTS should be tailored to individual patient needs and disease status, taking into account factors like mobility, cognitive function and general medical condition.**
- **Conservative management includes prompted voiding, toilet training and oral antimuscarinics.**



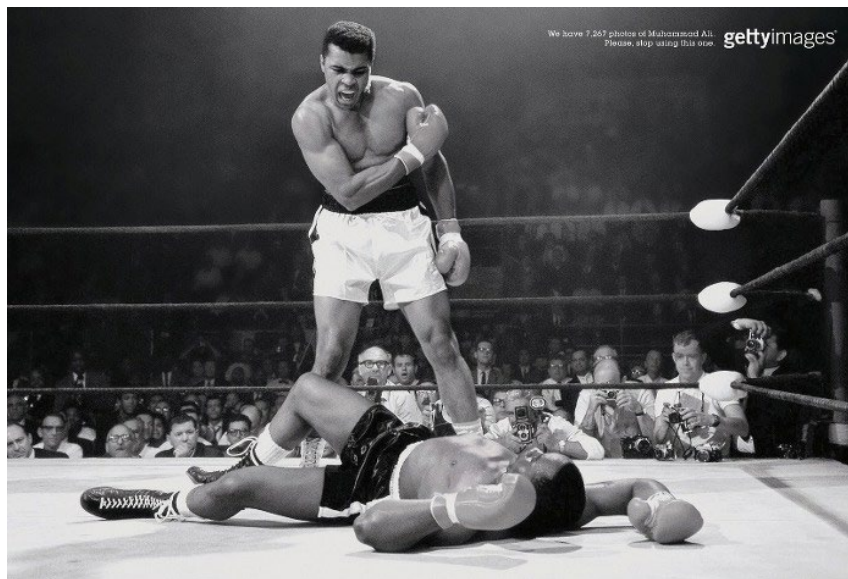
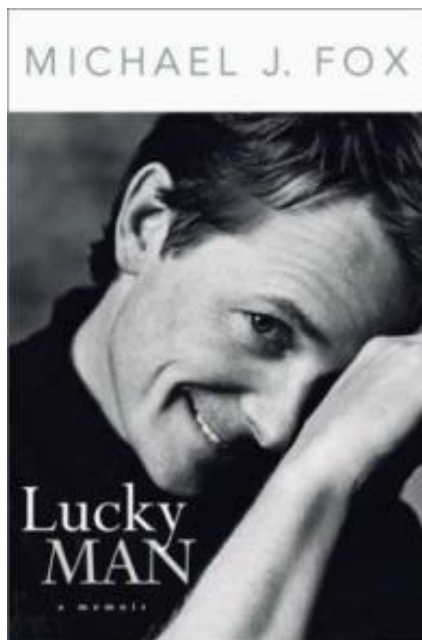
LUT dysfunction in patients with Parkinson's disease



James Parkinson

Surgeon

April 11, 1755



LUT dysfunction in patients with Parkinson's disease

- **Parkinson's disease**

- ✓ *Degenerative disorder associated with loss of dopaminergic neurons*
- ✓ *Overall incidence : 1/1000 (second most common degenerative neurological disease)*
- ✓ *motor symptoms : tremor, slow gait and easy fall*
- ✓ *Non motor symptoms : neuropsychiatric disorders, sleep disorders, sensory symptoms, and autonomic disorders (particularly OAB and constipation)*



LUT dysfunction in patients with Parkinson's disease

- LUTS in Parkinson's disease

- ✓ *Prevalence : 27% to 85% in any type of urinary symptoms (Mcdonald et al. 2016)*
- ✓ *Higher prevalence of voiding phase LUTS in male pts.*
- ✓ *Type of LUTS : filling phase (55%), voiding phase (11%), mixed (34%)*
- ✓ *Most frequency symptoms : Nocturia, Urgency, UI and weak stream*



LUT dysfunction in patients with Parkinson's disease

- **Urodynamic patterns**

- ✓ *D. overactivity* : 67%
- ✓ *D. underactivity* : 8%
- ✓ *Normal pattern* : 25%
- ✓ *DS dyssynergia* : 0-3%

- **Sphincter Bradykinesia**

- ✓ *The failure of the pelvic floor muscles and external urethral sphincter to relax rapidly before detrusor contraction*
- ✓ *Manifestation of skeletal muscle rigidity in the pelvic floor*



LUT dysfunction in PD – *the role of dopamine receptors*

- The different role of D1 and D2 dopamine receptors on lower urinary tract (LUT) behavior has been demonstrated in animal studies
- D2 agonists and D1 antagonists
 - bladder capacity ↓ micturation reflex ↑
- Hypothesis
 - ✓ D1 receptors : tonic inhibition of bladder voiding
 - ✓ D2 receptors : facilitation of micturition reflex
- Parkinson's disease is thought to result in underactivation of D1 receptors thus causing failure to inhibit the urination reflex.



LUT dysfunction in PD – anti PD drug and LUTS

- **The main pharmacological treatment of PD – Dopaminergic drug**
- **The role of dopaminergic medication in the management of LUTS is unclear**
- **The effects of dopaminergic treatment on bladder control is unpredictable**
- **The contrasting evidence are published and still on debate about the dopaminergic drug and their effect to LUTS in PD.**



LUT dysfunction in PD – *acute Vs. chronic effect*

- The acute L-dopa challenge significantly worsened bladder overactivity and bladder capacity
- However, the opposite results were seen in chronic administration.
- The acute and chronic L-dopa effects may be due to the different synaptic concentrations or to the activation of postsynaptic mechanisms obtained by chronic administration

Table 2 Urodynamic variables and lower urinary tract symptoms scored according to International Prostate Symptoms Score questionnaire

Urodynamic variables	Off treatment condition	First L-dopa challenge	L-dopa challenge during chronic treatment
Volumes			
First sensation, mL	129 ± 53	109 ± 73	240 ± 98**
NDOC threshold, mL	274 ± 146	186 ± 116*	319 ± 135 ⁺
Bladder capacity, mL	347 ± 122	269 ± 102*	360 ± 122 ⁺
Residual urine, mL	11 ± 20	2 ± 4	10 ± 26
Two-way ANOVA	Main factor treatment: $p < 0.001$		
	Post hoc: * $p < 0.001$ vs withdrawal condition, ** $p < 0.001$ vs first L-dopa challenge		



LUT dysfunction in PD – Urological treatment

▪ Medical treatment

- ✓ Overall treatment strategy is the same to the other neurophatic bladder
- ✓ Anti muscarinic agent – considering the BBB
- ✓ B3-agonist
- ✓ Alpha-blocker
- ✓ Desmopressin

▪ Surgical treatment

- PD with BPH – PD is not a contraindication to surgery
- Up to 70% success rate of BPH surgery in patients with PD

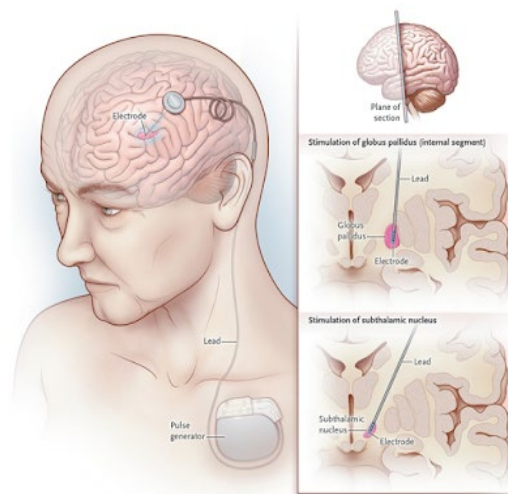
▪ Intervention - Botulinum



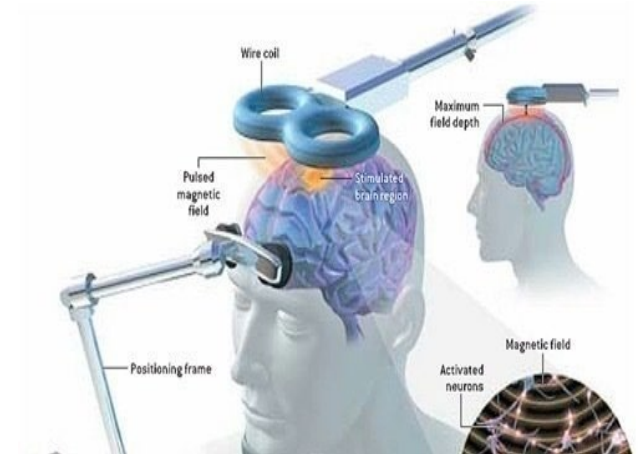
LUT dysfunction in PD : Non-urological treatment



Percutaneous Tibial Nerve Stimulation (PTNS)



Deep brain stimulation of subthalamic nucleus (STN-DBS)



Repetitive Transcranial Magnetic Stimulation (rTMS)



LUT dysfunction in Dementia – Summary

- **LUT dysfunction is common in PD**
- **Symptoms associated with overactive bladder predominate and their response to dopaminergic therapy remains uncertain.**
- **Studies have suggested that beta-3 agonist and Botulium toxin injection may have a role in addition to the classic bladder training and anticholinergic medication.**
- **The experimental trial included the electrostimulation therapy is emerging and showing the positive initial results.**

