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Brusa L[1], Petta F[2], Farullo G[3], Iacovelli V[3], Ponzo V[4], Iani C[1], Stanzione P[5], Finazzi Agrò E[2]
1. *UOC Neurologia, Ospedale Sant'Eugenio, Roma, Italia,* ***2.*** *Department of Experimental Medicine and Surgery, University Tor Vergata, Roma, Italia,* ***3.*** *School of Specialization in Urology, University Tor Vergata, Roma, Italia,* ***4.*** *Non-Invasive Brain Stimulation Unit, Neurologia Clinica e Comportamentale, Fondazione Santa Lucia IRCCS, Roma, Italia,* ***5.*** *Tor Vergata University, Dept. of Systems Medicine, Roma, Italy*

ROTIGOTINE EFFECTS ON BLADDER FUNCTION OF PARKINSON'S DISEASE

Hypothesis / aims of study

Lower urinary tract symptoms (LUTS), more frequently of the filling phase, are present in one to two thirds of Parkinson's Disease (PD) patients. The most common urodynamic finding in this patients' population is neurogenic detrusor overactivity (NDO) (1). Different effects of dopaminergic medication are reported in literature. Acute dopaminergic stimulation by L-dopa challenge has been reported to worsen NDO and reduce bladder capacity in PD patients. However, this data is conflicting with the clinical experience of bladder function improvement in PD patients during L-dopa therapy and confirmed other studies. A different role of D1 and D2 dopamine receptors has also been postulated (2).

In this study, we aim to assess the effects of Rotigotine (a dopamine agonist with a dopamine receptor profile well known to be distributed on D1 and D2 receptor) on bladder function in early mild PD patients that complained filling phase LUTS.

Study design, materials and methods

Twenty "de novo" patients (9M; 11F; mean age 62.0±3.2) with a late diagnosis of PD (mean disease duration in months 36.0±5.1) according with the Brain Bank Criteria 9 were enrolled in the present study. Inclusion criteria were represented by a complaining of urinary filling phase LUTS as urgency and increased day time/night time frequency defined according to the International Continence Society (ICS) definitions. Exclusion criteria were consumption of any drug acting on the central nervous system and/or on the LUT and history of urologic disorders. All patients were L-dopa and/or DA agonist naive.

All the subjects were evaluated with a first urodynamic session in off treatment condition, before the beginning of Rotigotine therapy. Then, a chronic Rotigotine patch mono-therapy was administered. Three months later, all patients accepted to undergo to a second urodynamic session. All patients were evaluated by the UPDRS (section III) (normal = 0 - worst = 108) and by the International Prostate Symptoms Score (IPSS) questionnaire administered in off treatment condition (see table 1) and during Rotigotine chronic treatment. The following urodynamic parameters were evaluated: first sensation of bladder filling (FSBF), bladder volume at appearance of the neurogenic detrusor overactive contractions ("threshold", NDOC-t), bladder capacity (BC), neurogenic detrusor overactive contractions amplitude (NDOC-a), bladder capacity (BC), detrusor pressure at maximum flow (Pdet@Qmax), maximum flow (Qmax) and post-void residual (PVR).

For Statistical analysis, a two-way analysis of variance (ANOVA) for repeated measures, was used. The Greenhouse–Geisser correction was used when required. The post hoc Tukey test was used when allowed. The effect of therapy on LUT symptoms, scored according to the IPSS questionnaire, as for UPDRS Section III scores, was evaluated using a Friedman ANOVA with treatment as main effect followed by a Wilcoxon post hoc when allowed.

Results

All patients were treated for three months with Rotigotine patches (median daily dose 10mg; range 8-16mg). Rotigotine administration significantly improved some urodynamic parameters in comparison to baseline. The post hoc analysis showed a significant improvement ($p < 0.001$) of mean bladder capacity increase, a mean first desire to void increment and a mean NDOC threshold increase. No effect was found on the voiding phase parameters. Lower urinary tract symptoms in basal condition were mild to moderate in all patients, according to the IPSS questionnaire score. The total IPSS score was significantly changed during Rotigotine treatment in comparison ($p < 0.0005$) to baseline (Wilcoxon test); in particular, filling phase symptoms were significantly decreased by Rotigotine administration, whereas voiding symptoms were unchanged. The UPDRS (Section III) score obtained on Rotigotine, as expected, was significantly lower showing a significant enhancement after drug administration in comparison to baseline condition. Results are summarized in table 1.

Table 1

Urodynamic Variables	**Baseline condition**	**Rotigotine condition**
First sensation, mL	125 ± 48	175 ± 67 *
NDOC threshold, mL	186 ± 82	248 ± 84 *
NDOC amplitude, cm H2O	24.0 ± 31.0	27.0 ± 27.0
Bladder capacity, mL	330 ± 126	390 ± 120 *
Pdet at Qmax, cmH2O	15.0 ± 8.0	21.0 ±11.0
Qmax, mL/s	36.0 ± 14.0	36.0 ± 14.0
Residual urine, mL	32 ± 34	14 ± 27
*Two-way ANOVA Main factor treatment: p <0.001 Post hoc: * p <0.01 vs basal*		
Questionnaires	**Baseline condition**	**Rotigotine condition**
IPSS Filling (max score 15)	11.3 ± 2.0	6.2 ± 3.2 *
IPSS voiding (max score 20)	4.5 ± 1.7	5.2 ± 2.3
UPDRS section III	29.0 ± 8.1	17.0 ± 4.0 *
Hoehn and Yahr stage	2.5 ± 0.4	
*Two-way ANOVA Main factor treatment: p <0.001 Post hoc: * p <0.001 vs basal*		

Interpretation of results

Our data showed urodynamic and clinical amelioration of LUTS following Rotigotine treatment in a group of mild Parkinson's disease patients paralleled by significant improvement on motor symptoms.

Previous study demonstrated the different role of D1 and 2 receptor on micturition reflex in PD, as the importance of a double and balanced D1-D2 agonism for a bladder function amelioration. The reported positive effect on urodynamic and IPSS variables seems to be due to the balanced action of Rotigotine on the two dopamine receptors subfamily, as supported by pharmacodynamics studies. The clinical improvement was related to a decrease of filling phase symptoms, whilst no effects were found on voiding phase symptoms. Similarly, some urodynamics findings recorded during the filling phase were changed under Rotigotine, whilst no changes were observed in voiding phase parameters. This finding could be also due to the selection of patients, all of whom reported filling phase symptoms as per inclusion criteria. Nevertheless, the urodynamic and clinical parameters observed during the voiding phase were almost completely unchanged.

Concluding message

Chronic Rotigotine treatment produced urodynamic and clinical amelioration of filling phase LUTS in a group of mild Parkinson's disease patients, paralleled by significant improvement on motor symptoms.

References

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Disclosures

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