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EFFECTS OF RASAGILINE ON LOWER URINARY TRACT BEHAVIOUR IN MILD PARKINSON'S DISEASE PATIENTS

Hypothesis / aims of study

It is well known that bladder dysfunction is one of the most common autonomic disorders (1) complained by Parkinson's disease (PD) patients. PD patients frequently (>60%) report storage lower urinary tract symptoms (LUTS), including nocturia, urgency, increased daytime frequency and urinary incontinence. Dopamine seems to play a central role and recent data (2) pointed out that l-dopa chronic administration, possibly due to the combined stimulation of both D1 and D2 receptors, may improve bladder capacity and volume at which micturition reflex is activated. Rasagiline, a new generation monoamino oxidases (MAO) inhibitor, may increase the amount of dopamine availability at synaptic level, by increasing endogenous dopamine.in humans. The aim of this study was to investigate Rasagiline effect on LUT behaviour in a group of early mild PD patients complaining storage LUTS.

Study design, materials and methods

Patients affected by idiopathic PD (table 1) according with the Brain Bank Criteria were enrolled for the present study. The study was approved by our local ethics committee, and all participants provided informed consent. Inclusion criteria were presence of storage LUTS; early- mild patients with Hoehn and Yahr score <2.5 who received indication to the use of Rasagiline. Exclusion criteria were use of any drug acting on the lower urinary tract; history of urologic disorders.
All patients were evaluated with IPSS questionnaire and urodynamic evaluation before and after two months of Rasagiline use (1 mg/day). All patients underwent a blind clinical evaluation using the Unified Parkinson's Disease Rating Scale (UPDRS) performed in coincidence with each evaluations.
IPSS and the following urodynamic variables were evaluated: first sensation of bladder filling, neurogenic detrusor overactive contractions (NDOC) threshold, bladder capacity, and post-void residual urine, all expressed in milliliters; NDOC amplitude and detrusor pressure at maximum flow (Pdet@Qmax), expressed in centimeters of water; maximum flow (Qmax; mL/second).

Results

Twenty patients were enrolled; their clinical data are summarized in table 1.
Rasagiline administration significantly ameliorated bladder volume measurements in comparison to baseline. The post hoc analysis showed a significant ($p< 0.001$) increase of bladder capacity (of about 16%) and of first desire to void (of about 34%). while significantly decreased residual volume (-53%).
Lower urinary tract symptoms in basal condition were mild to moderate in all patients, according to the IPSS questionnaire score (mean: 12.3 + 2.1) .The total IPSS score was significantly changed on rasagiline treatment in comparison ($p < 0.0005$) to baseline; in particular, filling (irritative) symptoms were significantly decreased by rasagiline administration. Results are reported in table 2.
The UPDRS (Section III) score obtained on rasagiline showed a trend to amelioration although not significant in comparison to baseline (27±17 vs 32 ± 10).

Table 1 Patients' clinical and demographic characteristics

Age (years) Mean± SD	67± 3.2
Sex	7M; 13 F
Disease duration (months) Mean± SD	±
Hoehn and Yahr stage	2.3 ± 0.8
UPDRS section III	32 ± 10

Table 2. Urodynamic variables and IPSS

Urodynamic Variables	Baseline condition	Rasagiline condition
First sensation, mL	118 + 53	158 + 42 *
NDOC threshold, mL	170 + 86	188 + 73
Bladder capacity, mL	290 + 98	337 + 115 *
Two-way ANOVA Main factor treatment: $p <0.001$ Post hoc: * $p <0.001$ vs basal condition and vs cistimev		
Pressure		
NDOC amplitude, cm H2O	55 ± 40	51 ± 42
Pdet at Qmax, cmH2O	30 ± 16	32 ±12
Two-way ANOVA Main factor treatment: n.s		
Flow		

Qmax, mL/s	15 ± 4	13 ± 3
One-way ANOVA	Main factor treatment: n.s.	

	Basal condition	Rasagiline condition
IPSS filling (max score 15)	12.3 ± 2.5	9.7 ± 1.1*
IPSS voiding (max score 20)	5.3 ± 2.1	4.2± 1.2
Friedman ANOVA	Main factor treatment: χ=18,52, p <0.0001 Post hoc: * p<0.01	

Interpretation of results

In the present study we observed an urodynamic and clinical amelioration of LUT symptoms following Rasagiline treatment in a group of mild Parkinson's disease patients. Moreover, an improvement although not significant was observed on motor symptoms scored with UPDRS section III, when patients were on the MAO inhibitor in comparison to baseline and placebo. The reported data are on line with previous studies performed on animals and human beings demonstrating that dopaminergic stimulation obtained with l-dopa or dopamine agonists, produces a bladder function amelioration.

It is possible hypothesize that the observed bladder function amelioration following Rasagiline was due to an increased dopamine level in particular acting at the anterior cingulate cortex and at the insula; previous imaging studies demonstrated a relevant density of D1 receptors at these sites (3).

Concluding message

In conclusion our data reporting a significant bladder function amelioration in patients treated with Rasagiline, are in line with the common parkinsonian patients' experience of the LUTS amelioration when adequately treated with l-dopa.

References

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Disclosures

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