ORIGINAL ARTICLE

Respiratory Muscle Performance and the Perception of Dyspnea in Parkinson's Disease

Paltiel Weiner, Rivka Inzelberg, Avi Davidovich, Puiu Nisipeanu, Rasmi Magadle, Noa Berar-Yanay, Ralph L. Carasso

ABSTRACT: ***Background:*** Pulmonary and respiratory muscle function impairment are common in patients with Parkinson's disease (PD). However, dyspnea is not a frequent complaint among these patients, although it is well documented that the intensity of dyspnea is related to the activity and the strength of the respiratory muscles. ***Patients and methods:*** We studied pulmonary function, respiratory muscle strength and endurance and the perception of dyspnea (POD) in 20 patients with PD (stage II and III Hoehn and Yahr scale) before and after their first daily L-dopa dose. Respiratory muscle strength was assessed by measuring the maximal inspiratory and expiratory mouth pressures (PImax and PEmax), at residual volume (RV) and total lung capacity (TLC) respectively. The POD was measured while the subject breathed against progressive load and dyspnea was rated using a visual analog scale. ***Results:*** Respiratory muscle strength and endurance were decreased and the POD was increased during the off medication period compared to normal subjects. There was a nonsignificant trend to an increase in PImax, PEmax and endurance after L-dopa intake. The POD of PD patients decreased ($p<0.05$) following medication, although, it remained increased ($p<0.01$) as compared to the normal subjects. Even if patients had spirometry data showing a mild restrictive pattern, before medication, both forced vital capacity (FVC) and forced expiratory volume $(FEV)_1$ remained almost identical after L-dopa intake. ***Conclusions:*** Patients with PD have higher POD, compared to normal subjects and this increased perception is attenuated when the patients are on dopaminergic medication. The change in the POD is not related to changes in respiratory muscle performance or pulmonary functions. A central effect or a correction of uncoordinated respiratory movements by L-dopa may contribute to the decrease in POD following L-dopa treatment.

RÉSUMÉ: La performance des muscles respiratoires et la perception de la dyspnée dans la maladie de Parkinson. ***Introduction:*** L'altération de la fonction pulmonaire et des muscles respiratoires est fréquente chez les patients atteints de la maladie de Parkinson (MP). Cependant, ces patients se plaignent rarement de dyspnée, bien qu'il soit bien connu que l'intensité de la dyspnée est reliée à l'activité et à la force des muscles respiratoires. ***Patients et Méthodes:*** Nous avons étudié la fonction pulmonaire, la force des muscles respiratoires, ainsi que l'endurance et la perception de la dyspnée (PD) chez 20 patients atteints de MP (stage II et III à l'échelle de Hoehn et Yahr) avant et après la première prise de L-dopa de la journée. La force des muscles respiratoires a été évaluée par la mesure buccale des pressions inspiratoires et expiratoires maximales (PImax et PEmax), au VR et à la CT respectivement. La PD a été mesurée pendant que le sujet respirait contre une charge progressive. Il évaluait sa dyspnée au moyen d'une échelle visuelle analogue. ***Résultats:*** La force des muscles respiratoires et l'endurance étaient diminuées et la PD était augmentée pendant la période sans effet médicamenteux par rapport à des sujets normaux. On a observé une tendance non significative à l'augmentation des PImax, PEmax et de l'endurance après la prise de L-dopa. La PD a diminué ($p<0.05$), tout en demeurant plus élevée comparée à celle des sujets normaux ($p<0.01$). Même si on observait un patron légèrement restrictif à la spirométrie des patients avant la prise du médicament, le CVF et la VEMS sont demeurés presque inchangés après. ***Conclusions:*** Les patients atteints de la MP ont plus de PD comparés aux sujets normaux et cette perception augmentée est atténuée quand les patients sont sous médication dopaminergique. Le changement de la PD n'est pas relié aux changements de performance des muscles respiratoires ou à la fonction pulmonaire. Un effet central ou une correction des mouvements respiratoire incoordonnés par la L-dopa peuvent contribuer à la diminution de la PD suite à l'administration de L-dopa.

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Parkinson's disease (PD) is a progressive extrapyramidal disorder characterized by bradykinesia, rigidity, tremor, and impaired postural reflexes.[1]

It has been shown that PD patients may have an array of respiratory abnormalities, such as reduced maximal inspiratory and expiratory flows,[2,3] upper airways dysfunction,[4] a restrictive pattern of pulmonary function[5] and diminished strength of the respiratory muscles.[6,7] Treatment with a dopamine-agonist consistently increased the strength of the muscles.[8]

Although these pulmonary and respiratory muscle function impairments are commonly reported in PD,[9-12] most patients do not report respiratory symptoms such as dyspnea. As a consequence of their sedentary life, the respiratory adaptation to effort is rarely used.

From the Department of Medicine A (PW, AD, RM, NB-Y) and Department of Neurology (RI, PN RLC), Hillel Yaffe Medical Center, Hadera, Israel

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Reprint requests to: Paltiel Weiner, Department of Medicine A. Hillel Yaffe Medical Center, Hadera, Israel 38100

Studies suggest that dyspnea, at least in part, is perceived as respiratory muscle effort[13,14] and it is well-documented that the degree of breathlessness, subjectively reported by the patients, is related to the activity and the strength of the inspiratory muscles.[15]

In order to evaluate the perception of dyspnea (POD) and how it is affected by the treatment, we studied the pulmonary functions, the respiratory muscle strength and endurance and the POD, in 20 patients with PD, before and after their first daily dose of L-dopa treatment and in 20 healthy matched control subjects.

Methods

Patients

Twenty consecutive ambulatory patients with long-standing PD (10 males and 10 females, mean±SEM age 66.2±2.2 years, stage II and III Hoehn and Yahr scale[16]), all naive to the purpose and the methodology of the study, participated in the study. Patients with known cardiac or chronic lung disease were excluded from the study. Their results were compared to twenty healthy age- and sex-matched subjects (10 males and 10 females). Motor evaluation used the Unified Parkinson's Disease Rating Scale (UPDRS).[17] All patients had chest x-rays taken and no patient had pulmonary or pleural fibrosis. Their characteristics are summarized in the Table. Written informed consent was obtained in all cases, and ethical approval for the study was granted by our hospital Human Ethics Committee.

Table: Patient characteristics

Patient	Sex	Age (y)	Severity Hoehn & Yahr	Motor UPDRS "off"	Motor UPDRS "on"	Duration of disease (y)
1	M	60	III	39	24	11
2	M	70	II	38	26	3
3	F	61	III	53	44	7
4	F	73	III	27	24	7
5	M	63	II	27	21	3
6	F	60	II	40	26	2
7	M	73	III	30	23	6
8	F	76	III	39	27	14
9	M	71	II	21	18	12
10	F	72	III	31	19	7
11	M	45	II	43	19	14
12	F	44	II	25	15	5
13	M	68	III	61	37	3
14	F	67	III	52	41	3
15	M	70	II	33	29	4
16	M	62	III	47	34	6
17	F	63	III	66	47	19
18	F	66	II	58	24	13
19	M	85	III	55	36	4
20	F	74	III	42	31	7
Mean		66.2		41.4	28.3	7.5
±SEM		±2.2		±2.9	±2.0	±1.1

UPDRS = Unified Parkinson's Disease Rating Scale (motor part). Higher scores reflect worse parkinsonian symptomatology

Measurements

All measurements were performed before ("off") and after L-dopa intake ("on"), on the same day, with the patients unaware of the purpose of the measurements, in all PD patients. Since L-dopa has a very short half-life and the fact that all patients were outpatients, we arbitrarily chose to assess the effect of the morning dose.

The patients were treated with 3-6 doses of L-dopa (mean±SEM dose 575±65 mg, range 375-750 mg).

Spirometry. Maximum expiratory and inspiratory flow-volume curves were measured at least three times, on a computerized spirometer (Compact, Vitalograph, Buckingham, England), according to the American Thoracic Society guidelines, and the best trial was reported. (The technician should demonstrate the appropriate technique. Have the subject inhale from functional residual capacity to total lung capacity (TLC), and then insert the breathing tube into his mouth, making sure his lips are sealed around the mouthpiece and begin the forced vital capacity (FVC) maneuver without hesitation. Prompt the subject to "blast" the air from his lungs, then continue to encourage him to fully exhale.)

Inspiratory and expiratory muscle strength. Inspiratory and expiratory muscle strength were assessed by measuring the maximal inspiratory mouth pressure (PImax) at residual volume (RV) and the maximal expiratory mouth pressure (PEmax) at TLC as previously described by Black and Hyatt.[18] The values obtained from the best of at least three efforts were used.

Inspiratory muscle endurance. Inspiratory muscle endurance was determined by using a device similar to that proposed by Nickerson and Keens.[19] Subjects inspired through a two-way Hans-Rudolph valve, the inspiratory port of which was connected to a chamber and plunger to which weights could be added externally. Inspiratory elastic work was then increased by the progressive addition of 25 to 100 g weights at two-minute intervals, as previously described by Martyn and coworkers,[20] until the subjects were exhausted and could no longer inspire. The pressure achieved with the heaviest load (tolerated for at least 60 s) was defined as the peak pressure (PmPeak).

Perception of dyspnea. The sensation of dyspnea was measured while the subject breathed through a device similar to that proposed by Nickerson and Keens.[19] Subjects inspired through a two-way Hans-Rudolph valve, the inspiratory port of which was connected to a chamber and plunger to which weights could be added externally. The subjects breathed against progressive loads, at one minute intervals, in order to achieve mouth pressure of 0 (no resistance), 5, 10, 20, and 30 cm H_2O. After breathing for one minute at each inspiratory load, in a protocol similar to the one that has been previously described by Kikuchi and coworkers,[21] the subjects were required to choose a number, using a modified Borg scale,[22] that represented the level of the perceived inspired difficulty, in which 0 indicated no difficulty and 10 the maximum difficulty.

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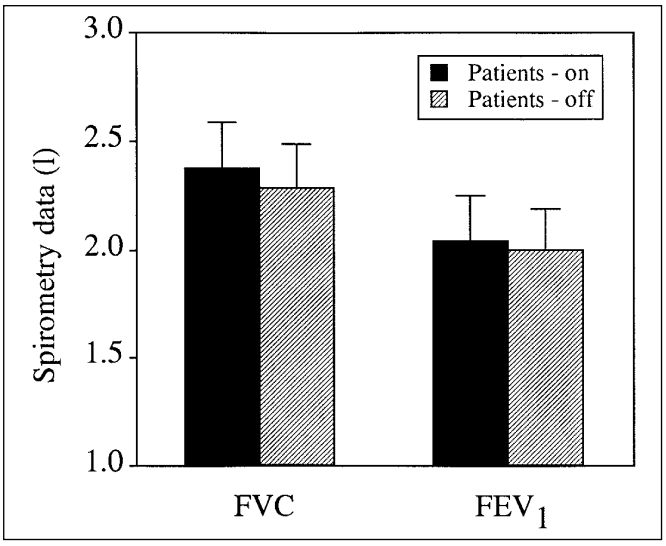


Figure 1: *Mean (±SEM) FVC and FEV_1 during the "off" medication period and during the "on" medication period in the PD patients.*

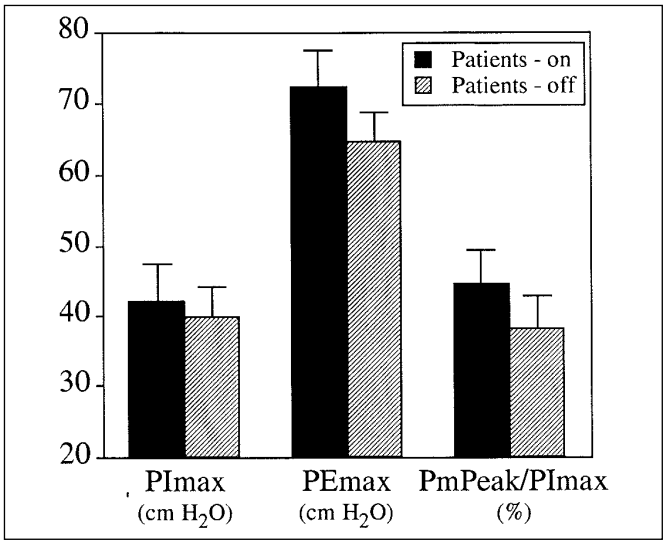
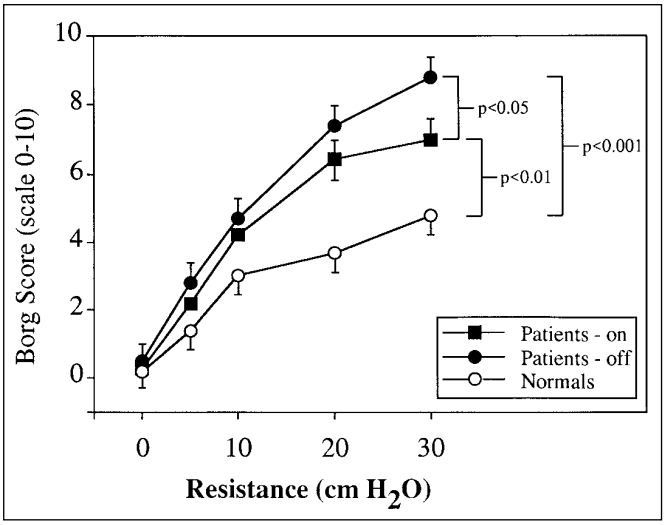


Figure 2: *Mean (±SEM) inspiratory and expiratory muscle strength and inspiratory muscle endurance during the "off" medication period and during the "on" medication period in the PD patients.*



Left:
Figure 3: *The perception of dyspnea, as was measured while the patient inspired against incremental resistance, during the "off" medication period and during the "on" medication period in the PD patients.*

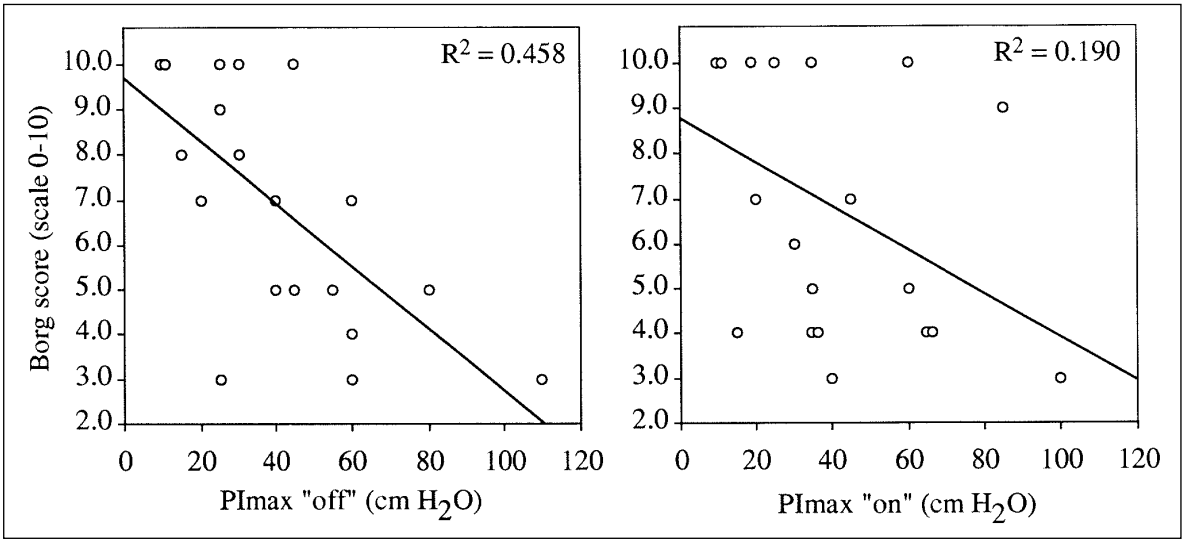


Figure 4: *The correlation between the inspiratory muscle strength and the perception of dyspnea during the "off" medication period and during the "on" medication period in the PD patients.*

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Data analysis

The results are expressed as means±SEM. Correlations were assessed by calculating Spearman correlation coefficients. Comparisons of lung function inspiratory muscle strength and dyspnea score were carried out using the Anova two-way repeated measures analysis of variance.

Results

Spirometry. Most patients had spirometry data showing a mild restrictive pattern (mean FVC=81.1±4.2% of predicted normal values). The mean ±SEM FVC was 2.28 ±0.2L during the "off" period and remained almost identical during the "on" period (2.37±0.2L). The mean forced expiratory volume $(FEV)_1$ was 1.99 ±0.2L during the "off" period and also remained almost unchanged during the "on" period (2.04±0.2L) (Figure 1).

Inspiratory and expiratory muscle strength and inspiratory muscle endurance. The mean inspiratory and expiratory muscle strength in the "off" period, as assessed by the PImax and the PEmax (39.8±6.2 cm H_2O – 45% of predicted and 64.5±7.2 cm H_2O – 57% of predicted), as well as the inspiratory muscle endurance, as assessed by the relation PmPeak/PImax (38.1% - 48% of predicted) were significantly decreased in the patients with PD. All these parameters of respiratory muscle performance tended to increase in the "on" period. However, this increase did not reach statistical significance (Figure 2).

Perception of dyspnea. The POD was significantly increased ($p<0.001$) during the "off" period as compared to normal subjects. It decreased significantly ($p<0.05$) when measured during the "on" period. Despite the improvement, POD remained greater than in the control normal subjects ($p<0.01$) (Figure 3).

There was a close correlation ($p<0.01$, $R^2=0.458$) between the inspiratory muscle strength and the POD in the "off" period. In contrast, during the "on" period this correlation was weakened and not significant (Figure 4).

Discussion

We showed that patients with PD have higher POD, as compared to normal subjects, and that this increased perception is attenuated after L-dopa intake. This change in the POD is not related to changes in respiratory muscle performance or pulmonary functions.

Although respiratory abnormalities are common in PD, dyspnea is not a frequent complaint suggesting that PD patients have a decreased POD. Alternatively, it may be that most patients probably do not report dyspnea, because their physical disability does not lead to activities where such problems can manifest themselves. Most of our patients had a mild restrictive pattern of pulmonary function (mean±SEM FVC=81±6.2% of predicted) with no significant inspiratory or expiratory flow limitation. As previously reported, the mean inspiratory and expiratory muscle strength, before and after dopaminergic medication, as well as the inspiratory muscle endurance, were decreased.[7,10] However, when the respiratory muscle strength was assessed with nonvolitional tests, it was clearly shown that both inspiratory and expiratory muscle strength were entirely normal.[23]

The effects of PD on respiration are still debated. Most reports of pulmonary function abnormalities in PD predate the era of L-dopa therapy which revolutionized the treatment of this disorder. Many investigators emphasized the presence of a restrictive pattern of impairment in PD,[3,24] and reported improvement of the impairment following treatment with L-dopa. Others have reported that a high percentage of PD patients present either upper or lower airway obstruction.[7] In all, mean airway resistance was in the normal range.[2] The reduction in the respiratory muscle strength in our patients is comparable to those reported by Bogaard and coworkers[25] and Tzelepis and co-workers.[6] Additionally, while some authors have shown improved respiratory function in PD with dopaminergic treatment,[4,8] others[2] did not find, as in the present study, any improvement in respiratory function with L-dopa. These discrepancies may be due to differences in patients' age, disease severity and measuring techniques.

Dyspnea was recently defined by the Medical Section of the American Lung Association as "subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity".[26] The pathophysiology of dyspnea is not completely understood. An attractive theory is that dyspnea results from a mismatch between central respiratory motor activity and incoming afferent information from receptors in the airway, lungs, respiratory muscles and chest wall structures.[27,28] This phenomenon may be similar to the sensory-motor mismatch observed in the function of limb muscles in PD.[29] The POD is an attribution process that incorporates the way in which an individual identifies and evaluates the symptoms and make interpretations about their causes and consequences. The significant improvement in the POD in our patients following treatment with L-dopa cannot be explained by improvement of pulmonary function or respiratory muscles and is possibly due to a central effect.

In conclusion, we showed that PD patients have an increased POD compared to normal subjects. Treatment with L-dopa resulted in a decrease in the POD, although it remained higher than in normal subjects. Since pulmonary function and performance was not altered by treatment, L-dopa may improve POD by correcting either central drive or thoracic and abdominal muscle coordination.

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