Original Article

Pulmonary function tests in patients with Parkinson's disease: A case-control study

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Abstract

Background: In Parkinson's disease (PD), morbidity and mortality are commonly caused by respiratory disorders from pulmonary function impairments. Aim: The study aims to evaluate pulmonary functions in a cohort of patients with PD in comparison with age- and sex-matched control.

Methods: Pulmonary function test (PFT) was conducted using the Spirolab Spirometry kit, and results of forced vital capacity (VC), forced expiratory volume 1 (FEV1), FEV1/VC, and peak expiratory flow rate (PEFR) were obtained from 78 PD patients and 78 healthy controls.

Results: A total of 78 patients and 78 age- and sex-matched control comprising 60 (76.9%) males and 18 (23.1%) females were evaluated. The mean age ± standard deviation of the patients were 62.32 ± 8.67 and 62.31 ± 8.66, respectively; the difference in their age was not statistically significant ($P = 0.993$). The majority (38.5%) of the patients was in stage II of Hoehn and Yahr of PD. Vital capacity (VC) in PD patients and control was 2.481 and 3.106; the difference was statistically significant ($P < 0.0001$). The mean FEV1 in PD patients and control were 1.887 and 2.494; the difference was statistically significant ($P < 0.0001$). The mean FEV1/VC percent in PD patients and control were 75.812 and 80.303; the difference was statistically significant ($P < 0.0001$). The mean PEFR in PD patients and control were 45.58 and 67.46; the difference was statistically significant ($P < 0.0001$). Considering PD arm of the study, with the exception of FEV1/VC, there was significant negative correlation between all the parameters of PFT and patients age (VC, FEV1, PEFR, $r = -422$ and $P = 0.0001$, $r = -391$ and $P = 0.0001$, and $r = -0.244$ and $P = 0.031$, respectively).

Conclusion: In this study, the values of the evaluated PFTs (VC, FEV1, FEV1/VC, and PEFR) parameters were significantly lower in PD compared with age- and sex-matched control.

Key words: Nigeria, Parkinson's disease, pulmonary function

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Introduction

Since its initial description in 1817, respiratory abnormalities have been noted in Parkinson's disease (PD) patients.[1,2] In PD, morbidity and mortality are commonly caused by respiratory disorders from pulmonary function impairments.[3] Though the effects of PD on respiration are still a subject of debate, the pulmonary dysfunctions probably occur as a result of impaired/poorly coordinated activity of the respiratory muscles.[4]

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In spite of the physiological evidence of potentially severe pulmonary dysfunctions, many patients with PD do not commonly report respiratory symptoms until the final stages of the disease. This impairment goes unnoticed, possibly because physical disability in PD often makes a patient lead a sedentary life and limits the activities where respiratory problems can become manifest.[3]

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Pulmonary function abnormalities in PD could be obstructive, which was attributed to an increase in parasympathetic activity[5,6] or restrictive, which was thought to significantly contribute to impairment in activities of daily living in patients with PD.[7]

We, therefore, undertook this study to evaluate pulmonary functions in a cohort of patients with PD in comparison with age- and sex-matched control.

Methods

This case-control study was conducted at the Murtala Muhammad Specialist Hospital (MMSH), a Tertiary Referral Center in Kano, North-Western Nigeria. Seventy-eight consecutive adult patients clinically diagnosed as PD cases were recruited from the neurology outpatient department of the clinic. PD was clinically diagnosed in accordance with the clinical criteria of the United Kingdom PD Society Brain Bank.[8,9]

All the patients were screened using a careful clinical evaluation. Patients with a history of lung disease, cardiovascular pathology, medication that might result in pulmonary dysfunction, and those unable to perform pulmonary function test (PFT) because of anatomical abnormalities as well as the patients who smoke or those with clinical sign of dementia were excluded. Seventy-eight apparently healthy age- and gender-matched nonsmoker volunteers selected from the patients' relatives were included as controls.

The severity of disability of the patients was assessed according to the scale of Hoehn and Yahr. (H and Y)[10] PFT was conducted using the Spirolab Spirometry kit (MIR USA, Inc.). To achieve the best results, patients were given careful instruction and good demonstration. Attentive care was taken to obtain full understanding and cooperation from the patients. Trial sessions were held to allow the patients to get used to the device before the actual test. Forced VC (FVC), forced expiratory volume 1 (FEV1) and the ratio of FEV in the first-second to VC (FEV1/FVC), and peak expiratory flow rate (PEFR) were obtained from the device.

PFT parameters were obtained in three trials per measure from all participants.

Analysis of data was done using GraphPad Prism (version 5.03, GraphPad Software, Inc. CA 92037 USA). All lung volumes were expressed as percentages of the values predicted. The normality of the numerical data was assessed using D'Augustino and Pearson Omnibus tests. Numerical data that were normally distributed were expressed as the mean ± standard deviation (SD). Comparisons of PFT parameters between patients and control subjects were performed using Student's independent sample *t*-test. Comparison of pulmonary function parameters across H & Y stage was conducted using ANOVA and Tukey's *post hoc* test. PFT parameters and age of the patients were correlated using Pearson's correlation. $P < 0.05$ was considered statistically significant.

Ethical approval was obtained from the Ethical Committee of MMSH.

Results

During the study period, 78 patients and 78 age- and sex-matched control comprising 60 (76.9%) males and 18 (23.1%) females in each arm were evaluated. The mean age ± SD of the patients were 62.32 ± 8.67 and 62.31 ± 8.66, respectively, the difference in their age was not statistically significant ($P = 0.993$). The median duration of PD was 2 years (range 0.25–16 years).

Fourteen (17.9%) had unilateral and 64 (82.1%) had bilateral PD. Twenty (25.6%) of the patients were treatment (levodopa-carbidopa) naïve whereas the remaining of the PD patients, all of whom were in "on" period, were taking levodopa-carbidopa at the time of the tests. The majority (38.5%) were in stage II of H and Y of PD as there were 14, 30, 8, 24, and 2 in H and Y stage I, II, III, IV, and V, respectively. However, none of the patients had complaints related to respiratory abnormalities. The mean VC in PD patients and control were 2.481 and 3.106; the difference was statistically significant ($P < 0.0001$). The mean FEV1 in PD patients and control were 1.887 and 2.494; the difference was statistically significant ($P < 0.0001$). The mean FEV1/VC percent in PD patients and control were 75.812 and 80.303; the difference was statistically significant ($P < 0.0001$). The mean PEFR in PD patients and control were 45.58 and 67.46; the difference was statistically significant ($P < 0.0001$) [Table 1]. This difference was irrespective of the H and Y stage of the PD patients. Using FEV1/VC <75% of normal value criterion, the obstructive pattern of ventilatory abnormalities was found in 46% of the patients. On further analysis, the mean difference of the lung function tests across H and Y stages was statistically significant for VC and FEV1. Figure 1a and b showed the result of ANOVA as well as *post-hoc* analysis of the lung function tests. Considering PD arm of the study, with the exception of FEV1/VC, there was significant negative correlation between all the parameters of PFT and the patients' age (VC, FEV1, PEFR, $r = -0.422$ and $P = 0.0001$, $r = -0.391$and $P = 0.0001$, and $r = -0.244$ and $P = 0.031$, respectively). Nonetheless, fair correlation was also recorded between age and PFT performance in the control group (VC, FEV1, PEFR, $r = -0.25$ and $P = 0.0041$, $r = -0.31$ and $P = 0.0049$, and $r = -0.28$ and $P = 0.0385$, respectively).

Table 1: Comparison of pulmonary function parameters between patients with PD (cases) and normal subjects (controls)

Variable	Mean (95% CI)		*P*
	Cases (n=78)	Control (n=78)	
VC (L)	2.4810 (2.3172-2.6448)	3.1058 (3.10577-2.9550)	<0.0001
FEV1 (L)	1.8871 (1.7518-2.0224)	2.4937 (2.3642-2.6231)	<0.0001
FEV1/VC × 100	75.8115 (74.1131-77.5099)	80.3026 (78.88-81.7276)	<0.0001
PEFR (percentage predicted)	45.58 (43.28-47.87)	67.46 (65.29-69.63)	<0.0001

PD=Parkinson's disease; VC=Vital capacity; FEV1=Forced expiratory volume 1; PEFR=Peak expiratory flow rate; CI=Confidence interval

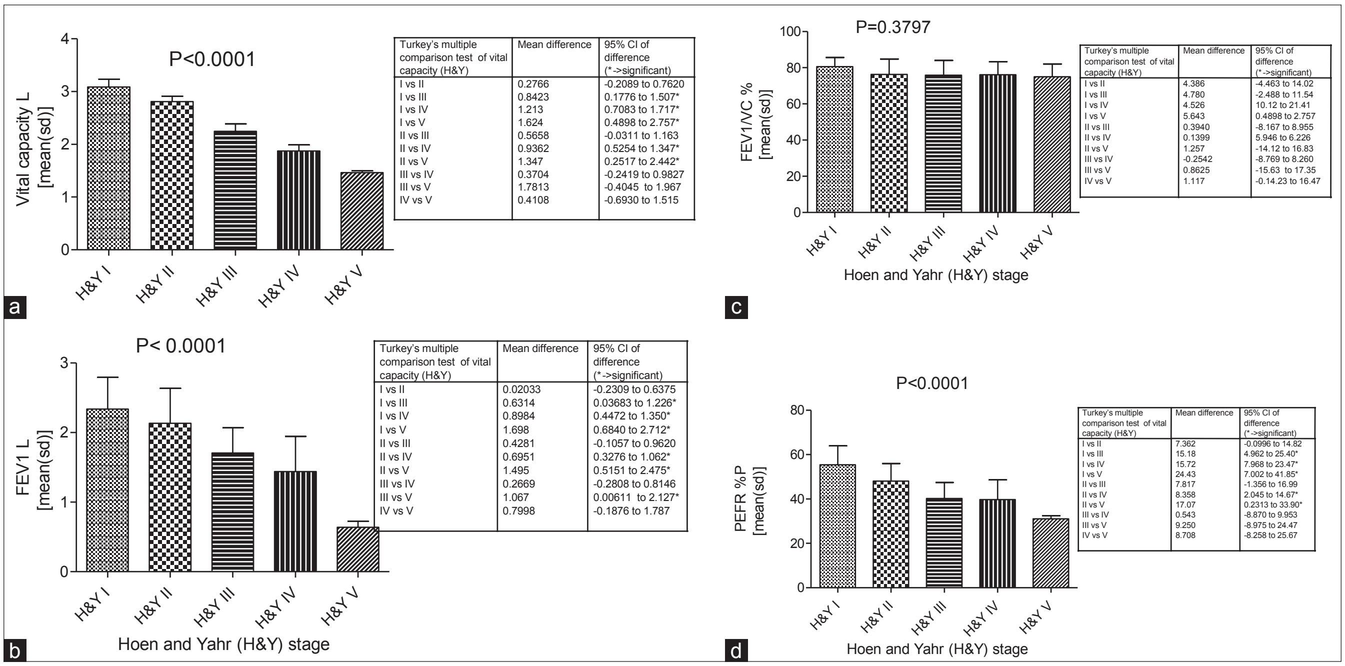

Figure 1: (a-d) Pulmonary function test results in Parkinson's disease patients according to disease severity

Discussion

In spite of the absence of respiratory symptoms in the PD patients in this study, values of all evaluated parameters were significantly lower in PD patients compared with age- and sex-matched control. This finding is in agreement with previous reports.[3,11,12] The low mean VC and FEV1 values can be attributed to external respiratory muscle rigidity and hypokinesia, which are prominent symptoms intrinsic to PD.[11] The other mechanisms suggested to have contributed to reduced lung volume and capacity in PD included increased parasympathetic activity,[13] coexisting chronic obstructive airway disease[14] or upper airway disease.[15]

Weiner et al.,[16] as well as De Keyser and Vincken,[17] based on the demonstration of dopaminergic cells in areas of the medulla known to control respiratory rate and depth, have proposed involvement of this anatomical site in respiratory disturbance in PD patients.[4,7,8]

Respiratory abnormalities are acclaimed to be a major cause of mortality in PD.[10]

Apart from restrictive change in respiratory function which is mainly due to chest wall rigidity, dopaminergic modulation-responsive upper airway obstruction which could result in both restrictive and dyskinetic ventilation and treatment with ergot derivatives which may also result in pleuro-pulmonary fibrosis, lung infection, which occurs as a consequence of disordered respiratory mechanics, continues to contribute significantly to morbidity and mortality in PD.[18] Owing to their relative immobility near the end of the disease spectrum, pneumonia is common and PD patients are 3–4 times more probable to die from pulmonary complications.[19]

Nevertheless the majority of the PD patients do not report respiratory disturbance, this discrepancy has been ascribed to the fact that the respiratory disturbance may go unnoticed while the disease develops, because physical disability from the disease may make PD patient lead a sedentary life, which indirectly limits the physical activities in which respiratory impairment could have become manifest.[11,12] Consequently, respiratory care becomes important when the patient becomes sedentary, and exercise training as a part of the pulmonary rehabilitation program has been found to be important in PD.[20]

Similar to reports from elsewhere,[21,22] we found an obstructive pattern of ventilatory abnormalities in 46% of our patients, however, it is worthy of note, that this was only based on ventilatory defect (FEV1/FVC <75% of normal value). Airflow limitation (maximal mid expiratory flow <65% of normal value), air entrapment (residual volume >120% of normal value) were not assessed in the current study, hence, interpretation and generalization of this finding should be done with caution.

Pulmonary function parameters were significantly smaller in patients with higher H and Y scale in comparison with those with lower H and Y scale. This finding is compatible with the report from the study conducted by Yamad *et al*. in which the values of %VC, %FEV1, FEV1/FVC, %PEFR, in H and Y IV group were significantly smaller than those in H and Y II and III groups.[23,24]

The negative correlation between the PD patients recorded in this study may be a reflection of the age-related functional changes in the respiratory system from progressive decrease in compliance of the chest wall in the static elastic recoil of the lung and in the strength of respiratory muscles that occur ordinarily in normal individuals with aging.[4] A similar finding in the control group in the current study further corroborated this explanation. However, the influence of this factor on the outcome of a comparison between PD patients and control was eliminated by matching the two arms by their ages.

In spite of our findings, our study had some limitations. Other pulmonary function parameters that are conventionally used to evaluate respiratory muscle strength, including the maximal inspiratory pressure, maximal expiratory pressure, and maximum voluntary ventilation that are sensitive indicators of neuromuscular disorders were not employed in the current study.

The findings in the present study have implications for the evaluation and treatment of individuals with PD particularly in Nigeria where PD is one of the most common neurological disorders.[25-27] Our findings suggest that PFT may serve as a useful indicator of assessment of lung function status in patients with PD. Thus, in such patients, implementation of lung function study could be rewarding in the areas of early detection and prevention of respiratory complications.

Besides, spirometry evaluation of PD patients could also serve as a useful tool for monitoring the effects of pulmonary rehabilitation programs on their respiratory dysfunction and quality of life. We suggest that the evaluation and rehabilitation of respiratory disturbances should be routinely included in the management of patients with PD. However, the intervention should be tailored to the individual's specific needs to improve pulmonary function.

Conclusion

In this study, the values of the evaluated PFT (VC, FEV1, FEV1/VC, and PEFR) parameters were significantly lower in PD compared with age- and sex-matched control.

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