Pulmonary function in Parkinson's disease

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SUMMARY Pulmonary function was investigated in 31 consecutive patients with relatively severe Parkinson's disease. Clinical disability was assessed by Hoehn and Yahr scale, Northwestern University Disability Scale and Websterscore. All patients were on levodopa substitution therapy and used anticholinergics. Pulmonary function was investigated by spirometry, determination of a maximal inspiratory and expiratory flow-volume curve and, when possible, maximal static mouth pressures were determined. Peak inspiratory and expiratory flow, maximal expiratory flow at 50% and maximal static mouth pressures were significantly below normal values. Vital capacity, forced inspiratory volume in 1 s and the ratio of forced expiratory volume in 1 s and vital capacity were relatively normal. Nine patients had upper airway obstruction (UAO) as judged by abnormal values for peak inspiratory flow, the ratio of forced expiratory volume in 1 s and peak expiratory flow and the ratio of maximal expiratory and inspiratory flow at 50%. Flow-volume curves were normal in eight patients; four patients demonstrated flow decelerations and accelerations (type A) and 16 had a rounded off flow-volume curve (type B). Type A can be explained by UAO and type B by a combination of decreased effective muscle strength and possible UAO. Overall results of pulmonary function tests in patients without any clinical signs or symptoms of pulmonary disease point to subclinical upper airway obstruction and decreased effective muscle strength in a significant proportion of patients.

Pulmonary function has been studied in Parkinsonism, including idiopathic Parkinson's disease.¹⁻³ Most studies were performed in the 1960s and were hampered by the fact that Parkinson's disease was not clearly separated from (post)-encephalitic Parkinsonism. Although Parkinsonism resembles Parkinson's disease in its main clinical features, there are also important differences, viz. absence of tremor and different course of progression. It was postulated, then, that there was in Parkinsonian patients concomitant chronic obstructive pulmonary disease³ or obstruction due to increased bronchial muscle tone caused by increased parasympathetic activity.²

In 1984 Vincken *et al*⁴ published their findings on pulmonary function in a variety of extrapyramidal disorders, including Parkinson's disease. They used the technique of maximal expiratory and maximal

inspiratory flow-volume (MEFV and MIFV) curve analysis and were able to distinguish two abnormal types of flow-volume curves. From this they concluded that upper airway obstruction (UAO) was the most prominent pulmonary abnormality.

Our study was aimed at the investigation of a possible relationship between UAO, as detected by flow-volume curves, and clinical disability in a homogeneous group of patients with relatively severe idiopathic Parkinson's disease. In addition measurement of maximal static mouth pressures was incorporated in the study in order to detect possible influences of impaired respiratory muscle function.

Patients and methods

Thirty one consecutive patients with Parkinson's disease were included in the investigation. The main inclusion criterion was the severity of the disease: according to the Hoehn and Yahr scale⁵ patients had to be at least in stage III. All patients were physically examined and had to complete a questionnaire about present and past health. Any history of lung disease that might have led to structural or functional pulmonary dysfunction or signs or symptoms suggestive of this led to exclusion. Other exclusion criteria were: use of

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Received 19 May 1988 and in revised form 24 September 1988.
Accepted 27 September 1988

Dr Meerwaldt died 31 December 1988.

Table 1 Patient characteristics

Hoehn & Yahr scale	III	IV	V	Total
N male	6	6	4	16
N female	6	5	4	15
N total	12	11	8	31
Age, males	60.5 (8.5)	65.5 (9.9)	64.6 (5.0)	64.6 (9.1)
Age, females	61.3 (11.8)	69.6 (4.5)	65.7 (4.0)	65.7 (8.9)
Age, all patients	60.9 (10.3)	67.4 (8.2)	65.1 (4.6)	65.1 (9.1)
Webster	15.1 (2.9)	18.9 (1.8)	24.9 (2.2)	19.0 (4.5)
NUDS	37.5 (2.8)	28.4 (6.5)	14.3 (5.1)	28.3 (10.4)
Duration (m)	82.5 (49.7)	88.4 (67.2)	101.3 (81.0)	89.4 (65.6)

In brackets: standard deviation.

medication which might result in pulmonary dysfunction, known structural abnormalities of the upper airways including oral cavity and dementia severe enough to interfere with pulmonary testing.

All patients were scored using Hoehn and Yahr,⁵ Webster⁶ and Northwestern University Disability Scale (NUDS)⁷ (see table 1). In addition age, age at onset of disease, principal symptom (tremor or rigidity) and medication were recorded.

All patients were on levodopa-substitution therapy. Furthermore all patients used anticholinergic drugs and some amantadine as well. Medication was not changed during at least one month prior to testing. The neurological parameters of all patients, including those who suffered from response fluctuations, were scored immediately before testing.

Pulmonary function testing

All patients were subjected to spirometry (Lode D 53/R, the Netherlands) which resulted in a measure of vital capacity (VC) and forced expiratory volume in 1 s (FEV₁). Always at least three attempts were made and the best result was used. A maximal expiratory and maximal inspiratory flow-curve (MEFV and MIFV) could be obtained in 28 patients. Of the remaining three, one patient could only produce a MEFV-curve, while the results in the two other patients were not reliable. The flow-volume curve relates maximal expiratory and inspiratory flows to displaced volume at the mouth from total lung capacity and residual volume during expiration and inspiration respectively. A normal example is given in fig 1. The following variables were derived:

PEF: peak expiratory flow

PIF: peak inspiratory flow

FVC: forced vital capacity

FIV: forced inspiratory volume in 1 s

MEF50 and MEF25: maximal expiratory flow after expiration of 50 and 75% of FVC and, for the inspiratory phase: MIF50. From these parameters the ratios FEV₁/PEF and MEF50/MIF50 were calculated.

In 22 of 31 patients (10 Hoehn and Yahr stage III, eight stage IV, four stage V) maximum static mouth pressure at residual volume (PMRV) and total lung capacity (PMTLC) could be measured accurately, according to the protocol of Black and Hyatt.⁸ Since a scuba-type mouth-piece was used, reference values were calculated following the guidelines of Vincken *et al.*⁹

For statistical analysis, besides Student's *t* test either Spearman or Pearson correlates were used, depending on the parameters examined. All *p* values are two-sided.¹⁰

Results

All pulmonary function parameters are expressed as percentages of normal values and are corrected for length, sex and age.^{8,11} For the peak inspiratory flow actual values are given as no reliable reference values are available. Since our group consisted of almost equal numbers of male and female patients and subgroup analysis showed no significant differences, only combined results will be given. They are tabulated in table 2. Significant differences from normal controls are indicated where they could be demonstrated. Maximum static mouth pressure at residual volume and total lung capacity (PMRV, PMTLC) and peak expiratory flow (PEF) (*p* < 0.01) and maximal expiratory flow at 50% (MEF50) (*p* < 0.05) were significantly below normal values. Numbers are too small to allow subgroup analysis, but

Fig 1 Normal MEFV-MIFV-curve. For abbreviations see text.

there is a trend for most parameters to decrease from group III to V. Vital capacity, forced inspiratory volume in 1 s and the ratio of forced expiratory volume in 1 s and vital capacity are relatively normal.

Twenty eight patients could produce a flow-volume curve. Four patients had a type A curve and 16 had type B, according to the classification of Vincken *et al*⁴ (see Discussion and fig 2). Three pulmonary function parameters can be regarded as indicators of upper airway obstruction (see also Discussion): peak inspiratory flow, the ratio of forced expiratory volume in 1 s and peak expiratory flow and the ratio of the maximal expiratory and inspiratory flow at 50%. Nine patients had an abnormal value for one of these parameters, eight patients for two and only one for all three parameters.

Several significant correlations (r) could be demonstrated between the neurological disability scores (Webster and NUDS) or the length of illness and the results of the pulmonary function test. They will not be given here as all r-values are rather small. They all

Table 2 Results on the pulmonary function tests

Hoehn & Yahr scale	III	IV	V	Total
VC	99.4	95.7	88.8	95.4
FEV1	98.3	98.4	79.5*	93.5
FEV1/VC	99.8	104.7	90.6	99.0
FIV1	110.6*	106.7	95.3	105.1
FVC	102.4	104.2	91.1	100.3
MEF25	89.8	97.2	95.4	93.7
MEF50	89.3	90.9	74.3	86.2*
PEF	98.3	83.4	61.3†	84.2†
PIF	5.1	3.9	2.9*	4.1†
PMTLC	41.9†	24.1†	29.5†	33.2†
PMRV	54.0†	34.2†	35.3†	43.4†
MEF50/MIF50	93.2	123.9	118.0	110.4

*Significance difference with normal controls $p < 0.05$.

†Significance difference $p < 0.01$.

For abbreviations see text.

remained well below the arbitrary value of 0.7. $r^2 \times 100$ is the percentage of the variation of one parameter caused by the other, and a r of 0.7 would result in 49%, a level indicating clinical relevance.¹⁰

Fig 2 A: type A flow-volume-curve and B: type B. See text for details.

Discussion

Respiratory problems are a major cause of death in patients with Parkinson's disease.⁵ Most patients do not, however, report respiratory problems, perhaps because their physical disability does not lead to activities where such problems can manifest themselves. Using modern techniques of pulmonary function testing it is possible to detect subclinical abnormalities and to localise them within the respiratory system. Several investigators have reported on respiratory abnormalities in patients with parkinsonism and several mechanisms were suggested: increased parasympathetic activity,^{1,3} coexisting chronic obstructive lung disease² and recently upper airway obstruction (UAO).⁴

In our group of patients, all with relatively severe Parkinson's disease and all without clinical signs or symptoms suggesting respiratory problems, two different kinds of abnormalities were found. Peak expiratory and inspiratory flows and maximal static mouth pressures at residual volume and total lung capacity were all significantly below normal values. The low mean pressure values can be explained by "muscle weakness" and hypokinesia, two symptoms intrinsic to Parkinson's disease. Peak expiratory and inspiratory flow are effort dependent variables from flow-volume-curves, but are moreover sensitive indicators of UAO.¹² In the upper airways the turbulence of the flow limits predominantly the largest flows produced, that is peak expiratory and inspiratory flow, which explains their sensitivity to upper airway narrowing.

Another kind of abnormality is the significant low value of maximal expiratory flow at 50%. This parameter is relatively independent of muscle strength¹² and can be attributed to UAO. Vincken *et al*⁴ mainly used the following criteria, for UAO: ratio of forced expiratory volume in 1 s and peak expiratory flow (FEV1/PEF) > 8.5 ml per litre per minute, ratio of maximal expiratory and inspiratory flow at 50% (MEF50/MIF50) > 1 and peak inspiratory flow (PIF) < 3 litres per second. These three criteria represent different aspects of an extrathoracic upper airway obstruction.

In the presence of such an obstruction, flow remains relatively small during the first part of the forced expiration. This results in a low peak expiratory flow (PEF). The integrated flow during the first second of forced expiration is much less sensitive to changes in PEF, which leads to a nearly normal forced expiratory volume in 1 s (FEV1).¹³ The net result is an increased FEV1/PEF ratio.

Inspiration leads to a lowering of the intraluminal pressure at the site of an obstruction. Since the obstruction is not anatomically fixed, this leads to an increase of the obstruction: maximal inspiratory flow

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at 50% (MIF50) decreases. The reverse process during expiration leads to an increased maximal expiratory flow at 50% (MEF50). The MEF50/MIF50 ratio is therefore increased to UAO. The same mechanism leads to a relatively low peak inspiratory flow during forced inspiration.

Because of the complex interactions of the mechanisms leading to these disturbances and the inter-individual variation which is already present in normal controls, the definition of UAO is in a certain way arbitrary. When one ignores one abnormal score, nine of our patients have two or more abnormal scores and can thus be considered to have signs of UAO.

The mentioned criteria can be considered as quantitative indices of UAO. The pattern of the flow-volume-curves can give a qualitative indication whether or not an UAO is present. Vincken *et al*⁴ have classified for this purpose the curves into three types (see fig 2):

1. Normal type
2. Type A. This consists basically of a normal pattern with superimposed de- and accelerations of the flow, either regular or irregular, which can be traced to tremor. Although the overall pattern is normal, often also lowered maximal flows are found.
3. Type B, which consists basically of a rounding off of the expiratory phase and a delayed appearance of the peak. In addition irregular flow changes occur frequently in the inspiratory phase.

In our group 82% of those with an abnormal curve had type B (n = 16), while only 22% of Vincken *et al*'s patients had this type and 78% type A. This discrepancy is probably caused by patient selection because a large proportion of their patients had tremor as a prominent symptom and also patients with only essential tremor were included.

The rounding off and the delayed appearance of the peak of type B can be explained by a decrease of the maximal effort, necessary for the flow-volume curve, and by UAO. The values for the effort dependent peak expiratory and inspiratory flow, as discussed above, are significantly below normal. Although this decrease can also be explained by UAO, the occurrence of this pattern also in cases with only a slightly lowered peak expiratory and inspiratory flow and the absence of a marked plateau in the curves points to "muscle weakness" as the basic mechanism. The markedly lowered maximal static mouth pressures at residual volume and total lung capacity provide additional evidence. Also hypokinesia will play a role in that it will lead to a less explosive effort and so cause a shift of the peak appearance to lower volume levels.

In our group four patients had a type A curve and all four had two abnormal parameters of the three discussed above (PIF, FEV1/PEF, MEF50/MIF50). This supports the concept of Schiffmann¹⁴ and Vincken *et al*,⁴ that a type A curve is indicative of

UAO. The very presence of deceleration of airflow indicates a narrowing. The flattened slope of the expiratory phase is additional evidence of UAO.

Since decelerations and accelerations of airflow are regular, it can be assumed that they are caused by tremor of the muscles of the upper airway. Aside from the tremor, obstruction can also be caused by the poor co-ordination of the muscles of the ventilatory system. Muscles of the upper airways have to be in phase with the muscles of the thoracic cage. It can be assumed that the extrapyramidal system plays a role in this co-ordination. Electromyography of the laryngeal muscles¹⁵ and videorecorded fiberoptic endoscopy of the upper airways⁴ lend some support to this hypothesis.

In patients with a type B curve the additive effects of UAO and "muscle weakness" are more difficult to separate due to the intrinsic qualitative nature of the derived parameters. We believe however that "muscle weakness" is the main determinant.

In our group we did not find any signs of increased parasympathetic activity or of chronic obstructive pulmonary disease. If the latter were the case, the ratio of the maximal expiratory and inspiratory flow at 50% would have been considerably smaller than 1 and the tail of the expiratory part of the flow-volume-curve depressed.

We conclude that there exist in relatively severe Parkinson's disease abnormalities of pulmonary function. They consist of a decreased effective strength of the respiratory muscles and of upper airway obstruction. This can lead to retention of secretion and possible subsequent infection. Due to patient selection none of our patients had any pulmonary complaints. That the pulmonary abnormalities remain subclinical can be explained by the fact that these patients are too disabled to perform any activities in which such abnormalities can manifest themselves. Since pulmonary function testing is relatively easy, non-invasive and sensitive it can be a valuable tool to detect these abnormalities.

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