INTRODUCTION

Respiratory dysfunction has been recognized as a cause of morbidity and mortality in patients with Parkinson’s disease (PD) (1-3). Respiratory complications, in particular aspiration pneumonia, are the most common causes of death in these patients (1,2).

A variety of respiratory problems such as aspiration pneumonia, respiratory dysrhythmias, which may or may not be associated with L-dopa therapy, chronic or recurrent airflow limitation, acute respiratory failure and lung infection, have been reported.

A REVIEW OF THE LITERATURE

Pulmonary function studies have yielded conflicting results in patients with PD. Obstructive and restrictive ventilatory defects, upper-airway obstruction and dysfunction, upper-airway and intercostal muscle involvement have been documented (1-7).

Hovestadt et al. reported that peak inspiratory flowrate (PIF), peak expiratory flowrate (PEF), force expiratory flowrate (FEF)50 and maximal static mouth pressure values were significantly below normal and vital capacity (VC), force expiratory volume in one second (FEV1)
and the ratio of force expiratory volume in one second to vital capacity (FEV<sub>1</sub>/VC) were relatively normal in patients with PD. Overall, their results of pulmonary function tests in patients without any clinical signs or symptoms of pulmonary disease pointed to subclinical upper airway obstruction and decreased effective muscle strength in a significant proportion of patients (8).

Izquierdo-Alonso et al. observed that abnormal flow-volume loop contour was a frequent finding in PD. They concluded that generalized airflow limitation was not an important characteristic of PD, by contrast, a restrictive spirometric defect was the main spirometric finding in these patients (9).

Bogaard et al. determined that only the effort-dependent variables PEF and PIF significantly correlated with severity of the disease and decreased with increasing clinical disability. The authors concluded that a decreased or less coordinated respiratory muscle force was a major feature in the decreased peak flow volume patterns (10).

Tzelepis et al. found essentially normal pulmonary function test results and infrequent impairment of maximal voluntary ventilation (MVV) in patients with either mild or moderate PD. They also demonstrated that patients with PD were able to perform single respiratory efforts well, but had difficulty performing repetitive inspiratory loaded ventilatory efforts. Pulmonary abnormalities have been explained by the global motor disability of these patients (11).

Vincken et al. (2) showed that the most common abnormality was an abnormal configuration of the flow-volume loop in patients with PD. Two abnormal patterns could be distinguished in this study. In the Type A pattern (“respiratory flutter”), regular consecutive flow decelerations and accelerations were superimposed on the general flow-volume loop (Fig. 1). The authors found the frequency of flow os-

Fig. 1 - Maximal expiratory and inspiratory flow-volume curves in patients with the Type A pattern, or respiratory flutter (Panel A), and patients with the Type B pattern (Panel B).

V<sub>ex</sub> and V<sub>in</sub> denote maximal expiratory and inspiratory flow rates, measured in liters per second (lps). V denotes volume (measured) in liters (2).
cillations to be similar to that of the tremor in the extremities. Endoscopy of the upper airway showed regular, rhythmic changes in the glottic area due to alternating abduction and adduction of the vocal cords and supraglottic structures.

The type B pattern was a grossly abnormal flow-volume loop with irregular, abrupt changes in flow, often dropping to zero. Endoscopy of the upper airways showed irregular, jerky movements of the glottic and supraglottic structures, frequently leading to sudden, intermittent airway closure.

Some of their patients had physiologic evidence of upper airway obstruction. They concluded that the intrinsic laryngeal muscles, and probably most of the other muscles surrounding the upper airway, are almost invariably involved in the involuntary movement characteristic of the extrapyramidal disorders.

This suggestion was supported by Vincken et al. in a case report (3). They found that there was an improvement of parkinsonian and respiratory symptoms following oral administration of L-dopa. This observation showed that extrapyramidal involvement of the striated upper airway musculature may limit airflow and cause respiratory symptoms.

Electromyographic abnormalities of laryngeal muscles have been reported in patients with PD (2,3). However, the authors did not comment on their respiratory implications. Twenty-four sets of striated muscles surround the upper airway and probably all of them have an automatic cyclic motor activity synchronized with the respiratory muscles. This respiratory activation promotes the stability and patency of the upper airway, and airflow resistance is greatly increased when the contraction of upper/airway muscles is out of phase with that of chest wall muscles. The upper airway and its musculature also have other important tasks: phonation, deglutition and protection of the lower respiratory tract. To accomplish all these activities it would seem that a well-developed extrapyramidal control system is essential.

The diaphragm seems to be spared in extrapyramidal disorders. EMG of the respiratory muscles in patients with PD showed that the diaphragm exhibited a close to normal activity (1-3).

Reduced vocal cord abduction and adduction, abnormal vocal cord movement amplitude and mucosal waveform, laryngeal tremor and oropharyngeal dysfunction have been observed in patients with PD by laryngoendoscopy and barium swallow videofluoroscopy (12,13).

The high incidence of serious chest infections in patients with PD may be explained by a cough reflex impairment: maximal voluntary cough (MVC) and reflex cough (RC) were analyzed in patients with PD, by monitoring the integrated electromyographic activity of abdominal muscles. In this study (14), patients with PD displayed a lower electromyographic activity of abdominal muscles during maximal expiratory pressure maneuvers (PE max), MVC and RC. The results indicated that RC is impaired in patients with PD.

It is also likely that upper airway dysfunction is an important factor in retained secretions, atelectasis, aspirations and respiratory infections (2).

The medications used to treat these conditions can also produce respiratory disease. Dyskinesias involving the respiratory muscles have been described in a variety of movement disorders, especially the tardive dyskinesia associated with long-term use of neuroleptic agents. The incidence of L-dopa induced dyskinesias is approximately 50% of patients treated, and is related both to the dose of L-dopa administered and to the duration of treatment.

It has been assumed that respiratory abnormality following L-dopa therapy may result from the choreiform movements or the rigidity-akinesia of respiratory muscle or from abnormal central control of ventilation (4,6). The respiratory disorder caused by L-dopa improves with reduction of the dose or discontinuation of the drug.

Vercueil et al. (1) investigated ventilatory changes after oral intake of L-dopa in order to
observe the mechanisms of the breathing impairment seen in patients with PD. They showed an attenuation of breathing discomfort in all patients following L-dopa administration. The main finding of their study was a lengthening of inspiratory duration (TI), a decrease in minute ventilation and an increase in the ratio of inspiratory time to total breathing time following the administration of L-dopa. Because of the observation of a normal diaphragmatic activity in patients with PD, they concluded that these changes in breathing pattern induced by L-dopa administration can be explained by changes in the activity of other respiratory muscles.

Intercostal muscles participate both in postural activity and in respiratory function. Differences exist in the extent of the contribution to respiration of internal and external intercostal muscles. In contrast to the external intercostal muscles, the internal intercostal muscles, which are mainly active during expiration, fulfill more of a ventilatory than a postural role. When activated by postural movements, the internal intercostal muscles were found to be strongly inhibited during inspiration, whereas the external intercostal muscles showed increases in inspiratory activity during postural muscular activity.

Thus, the changes in breathing pattern induced by L-dopa administration suggest that the respiratory dysfunction seen in patients with PD may be due to abnormal activity of intercostal muscles resulting directly from their state of rigidity, from an abnormal afferent discharge pattern or from dyskinesia.

Patients with PD typically demonstrate slowness in initiating and performing movement as well as reduced excursion of movement. Over time, parkinsonian patients tend to adapt to these changes and gradually reduce the amount and variety of regular physical activity they perform. Since extrapyramidal and pulmonary impairments make exertion unpleasant, these patients become sedentary. The resultant chronic inactivity deconditions the muscles of locomotion. This in turn makes physical activity even more unpleasant and thus reinforces the sedentary lifestyle. Therefore, these patients do not report pulmonary symptoms. This process of progressive disability can be depicted as a downward spiral (Fig. 2) (15).

Deconditioning and decreased endurance in the individual with PD have been discussed in many studies. The peak oxygen consumption (peak VO₂) and the peak heart rate (peak HR) reached during exercise are used to define the level of cardiovascular conditioning and to prescribe exercise. By interfering with the exercise movement, the PD-associated movement disorders of rigidity and bradykinesia can increase cardiovascular requirements, metabolic responses and ventilatory requirements for submaximal exercise.

Protas et al. (16) investigated cardiovascular and metabolic responses to upper and lower extremity exercise in patients with PD. Peak power was less in the PD group than in the control group and submaximal heart rate and oxygen consumption were higher in the PD group than in the control group. No differences were found between the groups for the other peak cardiovascular and metabolic responses (peak VO₂, peak respiratory exchange ratio (RER), peak HR). They suggested that the PD
group had lower efficiency during exercise and supported the need for exercise tolerance in all extremities.

Canning et al. (17) performed a study in order to evaluate the exercise capacity of subjects with mild to moderate PD and determine whether abnormalities in respiratory function and gait affect exercise capacity.

In this study, peak oxygen consumptions and peak work loads achieved by subjects with PD were not significantly different from normal values, despite evidence of respiratory and gait abnormalities typical of PD. Exercise category significantly correlated with percent predicted VO$_2$ peak, with sedentary subjects producing lower scores than exercising subjects. There was no significant correlation between disease severity and percent predicted VO$_2$ peak. The results suggested that individuals with mild to moderate PD who perform regular aerobic exercise may maintain normal exercise capacity, despite the presence of typical abnormalities in respiratory function and gait. The authors emphasized that patients with PD should be encouraged to perform regular aerobic exercise to maintain exercise capacity and quality of life.

Enhanced fatigue on performance of motor tasks and exercise intolerance are frequent complaints in patients with PD. Exercise intolerance and enhanced fatigue are characteristic of muscle mitochondrial impairment. A mitochondrial dysfunction has been observed in the substantia nigra of PD patients. It is still not clear whether there is a systemic (generalized extranigral) defect in mitochondrial function in parkinsonian patients, specifically in muscle tissue. Although such a defect has been found in several studies, it was not verified in others (18).

Ziv et al. (18) found a 50% increase in fatigue index (FI) in patients with PD. This increased FI was often asymmetric and more pronounced on the side more affected by the disease, and the FI improved significantly following oral intake of L-dopa. It has been suggested (18) that a systemic mitochondrial defect would result in a symmetric widespread enhancement of muscle fatigue. By contrast, these authors observed that muscle fatigue was asymmetric and correlated with the symptoms of the disease (i.e., rigidity and tremor). They concluded that PD fatigue has a possible association with central dopamine deficiency rather than with a muscle mitochondrial abnormality (18).

In another study (19), no striking differences in cardiovascular adaptation to physical work emerged in PD patients. The authors therefore proposed that it should be possible to improve cardiovascular endurance in PD patients, since their results did not support a clinically significant impairment of the respiratory chain.

Sabate et al. (5) investigated the effects of pulmonary dysfunction on activities of daily living (ADL) in patients with PD. Obstructive or restrictive pulmonary dysfunction and decreased arterial PO$_2$ were observed in their parkinsonian patients in comparison with controls. They showed that PD patients with respiratory dysfunctions suffered a greater deterioration in ADL than patients with normal pulmonary activity, although they had a similar degree of tremor, rigidity and bradykinesia. Thus, the results of this study suggested that the action of respiratory dysfunction on disability was not related to motor impairments. The authors also proposed that cervical and dorsal arthrosis and kyphoscoliosis, seen in PD, could lead to a reduction of thorax and vertebral column mobilization, facilitating the development of pulmonary restriction, and a decrease in vertebro-basilar blood flow (5). This suggestion had been previously been made by Shenkman and Butler (20).

In spite of the fact that most PD patients do not report pulmonary symptoms, the evaluation and rehabilitation of respiratory disorders should be systematically included in the daily management of these patients.
CONCLUDING REMARKS

Historically, pulmonary rehabilitation has been the cornerstone of the field of rehabilitation medicine. The first institutions of pulmonary rehabilitation, in the late 1940s and early 1950s, were devoted to the post acute rehabilitation both of patients with tuberculosis and of patients with neuromuscular respiratory paralysis (e.g., poliomyelitis). Today, the greatly increasing incidence of conditions analogous to tuberculosis and poliomyelitis, such as chronic obstructive pulmonary disease (COPD) and neuromuscular and spinal cord diseases, have once more increased the demand for pulmonary rehabilitation services.

Recently, pulmonary rehabilitation was defined as “a multidimensional continuum of services directed to persons with pulmonary disease and their families, usually by an interdisciplinary team of specialists with the goal of achieving and maintaining the individual’s maximum level of independence and functioning in the community” (21).

The multidisciplinary pulmonary rehabilitation team consists of a physiatrist and a pulmonologist, respiratory, physical, and occupational therapists, a psychiatrist or psychologist, a social worker, vocational counsellor, and a dietician. All the team members work together to personalize the patient’s treatment plan and to help improve the patient’s functional status.

Patients with COPD, restrictive lung disease, and sleep disordered breathing have been shown to benefit from pulmonary rehabilitation. Finally, there is a fourth clinical situation to which pulmonary rehabilitation principles can also be applied. In this situation, pulmonary dysfunction often complicates a variety of musculoskeletal, medical and central nervous system disorders, including traumatic brain injury, stroke, multiple sclerosis, and autoimmune deficiency syndrome. It is a frequent cause of morbidity and mortality and can hamp-er the rehabilitation of patients with these and other disorders. This situation has been little explored in the medical literature (21).

A variety of symptoms such as dyspnea on exertion, decreased exercise tolerance, difficulties during ADL, mood changes, hypoxemia, weight changes, and soft tissue pain have been recognized as signs prompting referral to a pulmonary rehabilitation program (22).

The components of pulmonary rehabilitation include an overall, multidisciplinary team assessment, exercise training, patient education, psychosocial intervention and follow-up. Therapeutic modalities in pulmonary rehabilitation focus on breathing retraining, airway secretion elimination, ADL, relaxation, energy conservation, nutrition, supplemental oxygen therapy and medication management (23).

Before entry to the pulmonary rehabilitation program, the following are performed or measured in order to assess the pulmonary rehabilitation patient:

- Pulmonary function testing (PFT)
- Chest radiograph
- Quality of life indicators
- Oxygen saturation
- Exercise testing.

PFT makes it possible to evaluate future changes in pulmonary status and lung disease, and helps to determine possible impairments, and to identify whether a patient has a restrictive or obstructive pattern.

A baseline chest radiograph will help identify the possible coexistence of pulmonary pathology (e.g., pneumonia or atelectasis).

Quality of life indicators such as the Sickness Impact Profile are important questionnaires to determine the patient’s overall status.

Oxygen saturation, via pulse oximetry at rest and with exercise, both with room air and with oxygen, may help to establish the need for oxygen supplementation.

Exercise testing is very important for accurate measurement of exercise tolerance and to demonstrate changes over time.
Outside the laboratory setting, exercise tolerance can be evaluated by means a simple test, such as a timed distance walk (e.g., a 6- or 12-minute walk). In the exercise laboratory, meanwhile, exercise performance can be quantified with greater precision by means of complex cardiopulmonary exercise testing. Treadmill or bicycle ergometry are acceptable cardiopulmonary exercise stress testing methods (23-25).

The exercise part of a comprehensive pulmonary rehabilitation program is perhaps the most important one. Many of the effects of pulmonary rehabilitation have been linked to the improvement of strength, endurance and the efficiency of the body’s muscle function.

The exercise program consists of reconditioning activities, upper extremity and respiratory muscle strengthening and breathing retraining.

Pursed lip breathing (PLB), air shifting and diaphragmatic breathing techniques are currently the three major controlled breathing (or breathing retraining) techniques and they are used widely. These techniques are employed to diminish dyspnea and increase the efficiency of the respiratory muscles.

The goals of controlled breathing techniques are:
1) To restore the diaphragm to a more normal position and function;
2) To decrease the respiratory rate by employing a breathing pattern that diminishes air trapping and improves the respiratory duty cycle;
3) To reduce the work of breathing;
4) To reduce dyspnea and allay patient anxiety (21,22,26).

Patients inhale through their nose for several seconds with their mouths closed; they then exhale slowly for 4 to 6 seconds through pursed lips held in a whistling or kissing position. The important responses to PLB have been observed to be an increase in tidal volume and a marked decreases in respiratory rate and minute ventilation. Other recognized benefits of PLB were reduced PaCO₂, and improved PaO₂ and arterial oxygen saturation (SaO₂) in resting patients with COPD.

Air shifting techniques involve taking a deep inspiration that is held with the glottis closed for 5 seconds, during which time the air shifts to lesser ventilated areas of the lungs. The subsequent expiration is via pursed lips. These techniques may be useful to decrease microatelectasis.

Possible benefits of diaphragmatic breathing exercises include improved lung mechanics, increased ventilatory efficiency and more even distribution of inspired gases. These techniques are usually initiated in the supine or 15% to 25% head-down position. The patient places his or her dominant hand on the upper-mid abdomen and the nondominant hand on the upper anterior chest. This makes it possible to monitor an inspiratory outward motion of the abdomen while minimizing chest excursions. The patient breathes more slowly and deeply, inspiring through the nose and expiring slowly through pursed lips. A conscious effort is made to employ only the diaphragm during inspiration and to maximize abdominal protrusion. Campbell et al. (see 26), noted that the early benefits of diaphragmatic type breathing included a major decrease in respiratory rate and in minute ventilation as well as an increase in tidal volume and reduced functional residual capacity. Several other groups had similar findings (26).

Ventilatory muscle exercises, including voluntary isocapneic hyperpnea, inspiratory resistive loading, and inspiratory threshold loading, can improve the strength and endurance of respiratory muscles (21,27,28).

In the techniques of isocapneic hyperpnea, the patient maintains as high a level of minute ventilation as possible for periods of 10 to 15 minutes, usually twice daily. These prolonged periods of hyperpnea ensure low tension and a high level of repetitive activity for the diaphragm and other inspiratory muscles.
In inspiratory resistive loading techniques, patients are required to breathe through inspiratory orifices of progressively decreasing diameter with the goal of increasing the load on the respiratory muscles. Breathing frequency during this type of training is generally kept within the range of 10 to 20 breaths per minute. However, it became apparent that many of the subjects of inspiratory resistive training consciously or unconsciously reduced their inspiratory flow rates and lengthened their inspiratory time to reduce the severity of the imposed loads (21).

In 1982, Nickerson and Keens (27) developed a threshold loading device that permitted inspiration to commence only after a threshold mouth pressure was reached. This type of training has been recommended to ensure adequate intensity of inspiratory muscle activity during training.

Many neck, arm and shoulder muscles are also accessory muscles of respiration. These muscles participate both in breathing activities and in the positioning or moving of the upper chest and upper extremity for ADL. The overlap in function explains why patients with lung disease are particularly short of breath when performing upper extremity ADL (15,21,29).

The mode of exercise in an upper extremity training program is usually arm cranking, but simple anterior elevation of the arms, gravity resistance exercises, swimming and rowing are also useful. It has been shown that training of the upper extremities results in improved performance for arm activities and in a drop in ventilatory requirements for upper extremity activity, such as raising the arms (15,29).

Equipment used for reconditioning exercise can include the treadmill, bicycle, and arm ergometer. In this type of exercise a starting level is found that is comfortable for the patient. If the activity causes a substantial increase in metabolic rate, and if the frequency, duration and intensity of the exercise are sufficient, an improvement in the aerobic performance of the muscle groups involved will be obtained. Intensity of exercise can be described using target heart rate, oxygen uptake, and the Borg rating of perceived exertion scale (Borg RPE scale) score. This indicator is usually scored from 0-10, with 0 indicating no discomfort or restlessness and 10 indicating extremely severe exertion or dyspnea.

The exercise sessions will often include at least 20 minutes (and preferably 30-60 min.) of continuous activity. An exercise session frequency of 3 to 5 days weekly is the goal for most pulmonary rehabilitation programs. A training program longer than 3 weeks (and preferably 5-10 weeks) is required to achieve a physiologic training effect (15,23).

A recent review of 48 pulmonary rehabilitation studies indicated that consistent improvements included decreases in the ventilatory equivalent or the ventilation/oxygen consumption ratio, increases in work efficiency (external work per unit of oxygen consumed) and, thus, in exercise tolerance, ambulation capacity, general well-being, dyspnea tolerance, and quality of life measures (21).

Few studies have investigated the effects of a pulmonary rehabilitation program on the respiratory dysfunction seen in patients with PD.

We observed (30) a slight improvement in flow volumes, lung volumes, ventilatory requirements (minute ventilation, VE; tidal volume, VT; and respiratory rate, RR) for the same respiratory effort and in ventilatory muscle force for the same repetitive respiratory maneuver after 5-week exercise programs aimed at improving ventilation. Also, there was a statistically significant increase in exercise tolerance and decrease in Borg RPE scale score at the end of the training program. Although we did compare some values statistically, our findings suggested that exercise training, as part of a pulmonary rehabilitation program for patients with PD, can decrease ventilatory re-
quirements for a given workload, increase ventila-
tory muscle force and exercise tolerance and improve the effort dependent spirometry variables and ventilatory pattern (larger VT, lower RR) during exercise.

The results from a small sample of patients suggest that exercise is a useful adjunct to pharmacologic therapy. Yet, these findings are an insufficient basis on which to conclude that exercise training, as a part of comprehensive pulmonary rehabilitation, can favorably affect the respiratory limitations seen in PD. Therefore, controlled studies in a larger group of patients are required to determine the effects of pulmonary rehabilitation in PD.

REFERENCES

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