Respiratory Response to Exercise in Postpolio Patients With Severe Inspiratory Muscle Dysfunction

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Objectives: To evaluate the limiting factors of exercise performance and to analyze the respiratory strategies adopted during exercise in postpolio patients with severe inspiratory muscle dysfunction.

Patients: Five patients with prior poliomyelitis associated with scoliosis and with respiratory muscle dysfunction (mean vital capacity, 1.74L [range, 1.1 to 2.4]) were studied at rest and during leg or arm cycle exercise.

Methods: Gas exchange was examined by arterial blood gases and mass spectrometry of expired air. Ventilatory mechanics were studied by measurement of esophageal and gastric pressures.

Results: Blood gases at rest were normal, except for subnormal P_O2 levels in three patients. In all but one patient, ventilatory insufficiency was the limiting factor for exercise. A compensatory breathing pattern with abdominal muscle recruitment during expiration was present already at rest in three of the patients. The pressures generated by the diaphragm were below fatiguing margins, ie, levels that in healthy subjects can be sustained for at least 45 minutes.

Conclusions: The extent of ventilatory dysfunction was not evident in blood gas values at rest; however, it was revealed by blood gas values during the exercise test. Diaphragm fatigue seems to be avoided at the cost of impaired blood gases.

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Respiratory deterioration may appear many years after acute poliomyelitis and has been reported in patients with or without a history of ventilatory support during the acute phase of the illness. Patients with neuromuscular diseases can develop ventilatory failure if their vital capacity is about 50% or lower than predicted. Besides the state of the respiratory system, metabolic demands are important in the development of respiratory failure. Ambulatory individuals require better ventilatory function during daily life than those who have extensive paraparesis and are confined to wheelchairs and whose sedentary life consequently might mask their ventilatory impairment until increased demands appear, as during infectious conditions.

Previous studies on respiratory function in late postpolio have mainly focused on sleep-related breathing disorders and pulmonary function during daytime and at rest. There have been few exercise studies on patients with prior poliomyelitis. In most of these exercise studies, arterial blood gases and ventilatory mechanical parameters, such as pressures and chest wall configuration, were not examined. A single case study was performed with arterial blood gas measurements during exercise by Frago and colleagues, who showed the effect of tracheotomy on exercise capacity in a postpolio patient with vocal cord paralysis.

Knobl and colleagues investigated respiratory mechanics during exercise in one postpolio patient with tracheal stenosis but did not analyze arterial blood gases. Shneerson investigated patients with scoliosis, some of whom had a history of prior poliomyelitis, and observed that in 80% of the patients exercise tolerance was limited by ventilatory factors. Sinderby and coworkers studied respiratory mechanics during exercise, but did not examine gas exchange parameters, and found that patients with cervical cord injury had a lower sensation of respiratory effort than postpolio patients.

To our knowledge no studies have been performed on postpolio patients with respect to both ventilatory gas exchange and ventilatory mechanics. The aim of this study was (1) to evaluate the limiting factors of exercise performance and (2) to analyze respiratory strategies at increased ventilatory demands in postpolio patients with severe respiratory muscle impairment, by examining gas exchange and ventilatory mechanics in five patients undergoing submaximal exercise tests.

METHODS

The selection of the patients for the study was based on symptoms of respiratory muscle impairment, vital capacity reduction, and the varying extent of extremity paraparesis.

Five men with prior poliomyelitis (mean time since acute infection, 41 years) gave informed consent to participate, and the study was approved by the local ethical committee. Patient data are presented in table 1.

One patient (patient 4) had required assisted ventilation with an iron lung during his acute poliomyelitis. Two patients (patients 1 and 4) had a history of late-occurring acute respiratory failure preceding the ventilator supply. Patient 1 had two episodes (P_O2 5kPa, P_CO2 6.8 and 8.0kPa) considered not triggered by infection, in contrast to patient 4, who had one episode (P_O2 5.3kPa, P_CO2 8.5 kPa; adding oxygen 1L/min increased the P_CO2 to 13.3 kPa) that presumably was associated with infection. Polysomnographic recordings showed hypventilation in two patients (patients 1 and 4) and obstructive sleep apnea in one patient (patient 5), and were normal with respect to pulsoxymetry and sleep architecture in two patients (patients 2 and 3). All patients were prescribed noninvasive positive pressure ventilation for nocturnal use, but patient 3 only used it...
partly in the daytime. Three patients (patients 1, 3, and 4) had preventrilator symptoms of general fatigue, one patient (patient 2) of increasing exertional dyspnea, and one patient (patient 5) of daytime tiredness.

Procedures

The five patients were examined on three occasions: a pretest, a test for gas exchange, and a test for ventilatory mechanics. The pretest performed to establish the highest workload (Wmax) (table 2) that could be sustained for 4 minutes, by increasing the workload in steps of 4 minutes with resting periods of 5 minutes in between. Those three patients whose upper extremity muscles were stronger than their lower extremity muscles performed arm ergometry and the other two performed leg exercise on a bicycle ergometer. Estimation of perceived limb and breathing effort was registered by using a Borg scale, ranging from 6 to 20.

Ventilatory gas exchange was studied at rest and during exercise. The workloads used as target levels (table 3) were somewhat lower than the maximal workloads (table 2) that could be sustained for 4 minutes found in the pretest. The lower workloads were used to reach a steady state and to get sufficient time for the collection of expiratory air. After a 1-minute warm-up period on a load corresponding to 20% of Wmax for 120 seconds (except for patient 3 with a load corresponding to 50% of Wmax), the patients exercised at the target levels until exhaustion. Samples for blood gases and lactate were obtained through a catheter in the radial artery, except in patient 2, from whom the samples were taken by an arterial puncture at rest and again immediately after work, followed by a set of repeated samples at 2-minute intervals for 10 minutes. In the other patients, samples for blood gases and lactate were collected at rest, during the later part of the exercise, and after exercise as in patient 2.

Blood gases were analyzed with an IL 1312 blood gas manager and lactate in neutralized perchloric extracts of whole blood by an enzymatic method. Expired air was collected in a Douglas bag connected to a valve with a dead space volume of 80mL. Oxygen and carbon dioxide concentrations were analyzed using a mass spectrometer, and stored in a digital computer.

For the ventilatory mechanics, an esophageal catheter with a balloon system was introduced via the nose. Pressure correction for the small lumen catheter was made according to Sinderby and colleagues. The most proximal balloon was positioned in the lower esophageal region to measure the esophageal pressure. The middle balloon functioned as an anchor beneath the cardia of the ventricle. The most distal balloon was placed in the stomach to measure the gastric pressure. The force generated by the diaphragm, the transdiaphragmatic pressure (Pdi), was calculated as the difference between the mean gastric pressure swing and esophageal pressure swing. The catheter was connected to two differential pressure transducers (Screen-MateSpezial®) for esophageal and gastric pressures. Flow was measured at the mouth with a pneumotachograph (Jaeger Screenmate, l/E 0586, resistance 36Pa/L/sec) and was time integrated to volume. Time for inspiration/time for the whole breathing cycle (Ti/Ttot) was calculated from the flow signal. The tension time index (TTdi) was calculated as the product of Ti/Ttot and the Pdi/Pdimax for each breath. The signals were analog-to-digital converted, processed, and stored in a digital computer.

Maximal inspiratory efforts against closed airways were performed to establish the Pdimax value. The patients had a visual feedback of the Pdi levels on a monitor. The ventilatory mechanics were studied during rest for 30 seconds, during a warm-up period with a load corresponding to 20% of Wmax for 120 seconds (except for patient 3 with a load corresponding to 50% of Wmax, due to the low Wmax). The patients then continued on Wmax until exhaustion and thereafter the registration continued for 120 seconds of recovery.

RESULTS

The perceived effort according to the Borg scale at the end of the maximal workload that could be sustained for 4 minutes is shown in table 2.

Gas Exchange Data

The respiratory data at rest and during exercise are summarized in table 3. At rest the blood gases were within the normal range in two of the five patients (patients 2 and 4). The other three had subnormal PaO2 levels. There was no indication of increased dead space ventilation. The alveolar-arterial PaO2 differences (P(A-a)O2) did not exceed 30mmHg.

During exercise, dead space ventilation exceeded normal levels in one patient (patient 2). During exercise the P(A-a)O2 was above normal (>35mmHg) in two patients (patients 1 and 5) and borderline in one patient (patient 4). Figure 1 shows that during exercise the tidal volume increased to about 45% to 60% of vital capacity in all but two patients (patients 3 and 4). One of them already had a tidal volume to vital capacity ratio above 60% while breathing at rest. The breathing frequencies at rest ranged from 8 to 30 breaths/min and increased during work to 21 to 60 breaths/min.

Minute ventilation and oxygen uptake, shown in figure 2, were appropriate to the performed leg workloads. The minute
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Table 3: Blood Gas Values Obtained At Rest and During Exercise

<table>
<thead>
<tr>
<th>Patient</th>
<th>Workload (watts)</th>
<th>pH Rest/Exercise</th>
<th>PO2 (mmHg) Rest/Exercise</th>
<th>PO2 (mmHg)</th>
<th>SaO2 (%) Rest/Exercise</th>
<th>VD/VT Rest/Exercise</th>
<th>P(A-a)O2 (mmHg) Rest/Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>75</td>
<td>7.38/7.24</td>
<td>43/56</td>
<td>71/47</td>
<td>94/74</td>
<td>.28/.28</td>
<td>21/46</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>7.45/7.40</td>
<td>33/33</td>
<td>83/84</td>
<td>97/86</td>
<td>.41/.35</td>
<td>24/24</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>7.40/7.40</td>
<td>42/39</td>
<td>71/80</td>
<td>94/86</td>
<td>.43/.1</td>
<td>23/19</td>
</tr>
<tr>
<td>4</td>
<td>30</td>
<td>7.39/7.33</td>
<td>43/44</td>
<td>77/65</td>
<td>95/61</td>
<td>.42/24</td>
<td>27/34</td>
</tr>
<tr>
<td>5</td>
<td>60</td>
<td>7.41/7.38</td>
<td>42/44</td>
<td>74/74</td>
<td>95/84</td>
<td>--/.25</td>
<td>27/39</td>
</tr>
</tbody>
</table>

Abbreviations: PO2, arterial oxygen tension; SaO2, arterial oxygen saturation; VD/VT, functional dead space volume/tidal volume; P(A-a)O2, alveolar-arterial oxygen tension difference.

Ventilation and oxygen uptake responses for the arm ergometry loads were also in the range of normal values. In four of the patients the lactate levels were markedly elevated with respect to the normal range (fig 2C). Three patients (patients 1, 4, and 5) reached their anaerobic threshold, as judged by their lactate levels and the decrease in base excess. One patient (patient 2) was close to his anaerobic threshold and one patient (patient 3) did not reach his anaerobic threshold. The three patients that reached their anaerobic thresholds did not adequately increase their minute ventilation in response to their increased lactate levels and thus did not decrease their PCO2 levels.

During exercise, PCO2 values (Fig 2D) increased markedly in one patient (patient 1) and to some extent in two patients (patients 4 and 5). One patient (patient 5) had a higher PCO2 value after the exercise had ceased, 45mmHg at 2 minutes and 46mmHg at 4 minutes after work compared with 44mmHg during the test. PO2 levels decreased during exercise in three patients. The blood gases from patient 2 were taken immediately after the run, which may have concealed a decrease in oxygen levels, but probably would not have affected the PCO2 because the other patients’ PCO2 levels remained constant or elevated after the exercise run.

Heart rate reserve, defined as predicted maximum heart rate minus heart rate at maximum work, was 37, 59, 67, 22, and 22 beats/min for patients 1 through 5, respectively. The breathing reserve, defined as maximum voluntary ventilation minus minute ventilation (L/min), at maximum ventilation was indirectly calculated as the expired volume of the first second (FEV1) of the forced vital capacity times 40 (FEV1 × 40) minus minute ventilation and was 14, 8, 59, 19, and 40L/min for patients 1 through 5, respectively.

Ventilatory Mechanics

The Pdimax value was 73, 61, 65, 70, and 85cmH2O for patients 1 through 5, respectively. As shown in figure 3, Ti/Ttot increased during exercise in two patients (patients 2 and 4) and to a minor degree in one patient (patient 3). Ti/Ttot was not changed in patient 5. Pdi/Pdimax increased in three patients (patients 1, 3, and 4) and to a very small extent in one patient (patient 5). Pdi/Pdimax decreased in one patient (patient 2).

The TTdi, calculated as the product of Ti/Ttot and Pdi/Pdimax, increased in four patients, two of whom had only a minor increase (patients 1 and 5). In one patient (patient 2) the TTdi decreased. All subjects were well below the fatigu
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Fig 3. Plot of inspiratory time/whole breath time (Ti/Tot, relative units) and transdiaphragmatic pressure/maximal transdiaphragmatic pressure (Pdi/Pdimax, relative units), showing the tension time index (TTdi = Pdi/Pdimax • Ti/Ttot) at rest (●) and TTdi during exercise (arrows) for each subject. The shaded area corresponds to the fatiguing level of an TTdi of .15.

Figure 4 demonstrates in all patients a decreasing contribution of gastric pressure to the Pdi during exercise compared with breathing at rest. In one patient (patient 3) this was less pronounced, probably because of the maintenance of positive gastric pressure during exercise in this patient. The other patients showed negative gastric pressure swings, at least during part of the inspiration. In three patients (patients 1, 4, and 5) the pattern of a decrease in gastric pressure during the initial part of inspiration with a late increase in gastric pressure was already seen during resting breathing, as exemplified by the data from patient 1 shown in figure 5. Patient 2, whose Pdi/Pdimax and TTdi decreased during work, had marked negative gastric pressure swings during exercise (fig 5).

 DISCUSSION

Breathing was the limiting factor for exercise performance in all but one patient (patient 3). In two patients (patients 1 and 2) this was demonstrated by the perceived effort of breathing combined with marked blood gas impairment (patient 1) and the high breathing frequency (patient 2), and in two patients by increased Pco2 levels despite high lactate levels. In one patient (patient 3) exercise was not limited by respiratory factors. This patient was able to perform only minor work because of weak extremity muscles.

All patients had a breathing reserve of >11L/min, as
calculated from the FEV$_1 \times 40$, except for patient 2 who had a reserve of 8L/min. However, in three patients (patients 1, 2, and 4) in whom a maximum ventilatory ventilation test was performed, the maximum voluntary ventilation showed no breathing reserve. In these three patients, maximum voluntary ventilation was 32, 35, and 24L/min, respectively, compared with the minute ventilation during the exercise test of 30, 35, and 23L/min, respectively, indicating that they had reached their ventilatory limits.

Despite the possibility of technical problems and poor performance, the discrepancy between the FEV$_1 \times 40$ and the maximum voluntary ventilation results might be interpreted as an indication of a decreased endurance of the respiratory muscles, which implies that the FEV$_1 \times 40$ should be used with caution for calculation of the breathing reserve in patients with weak respiratory muscles due to neuromuscular disease.

The observed lactate levels were higher than expected for the observed minute ventilation, oxygen uptake, and the external work performed, which could have resulted from several factors, such as sedentary life, small muscle groups performing the work, and a reduced elimination of lactate. The lactate levels for arm ergometry are known to be higher for a given workload than the lactate levels for leg ergometry. However, the lactate level was higher than expected for two of the patients performing arm ergometry. Another cause for the disproportionately high lactate levels could be the cost for the work of ventilation found in healthy subjects during sustained maximum voluntary ventilation. The presumably decreased compliance of the respiratory system in the patients in this study would probably cause an increased load on the respiratory muscles and thus might have contributed to the increased lactate levels. The influence of lactate levels, however, has been found to be insignificant for respiratory muscles in patients with chronic obstructive pulmonary disease (COPD).

The Pdimax values were low for all patients, indicating impaired diaphragm function. All patients showed expected changes in pressure patterns during the test with decreasing gastric pressure and increasing esophageal pressure indicating recruitment of intercostal and probably accessory breathing muscles, although we did not measure chest wall and abdominal movements. The observed increase in gastric pressures during at least part of expiration, most marked in patients 1 and 2, indicated a recruitment of abdominal muscles. Findings in normal subjects suggest that enhanced expiratory muscle activity occurs during exercise and decreases the functional residual capacity and increases the expiratory flow relative to the inspiratory flow. Maximum voluntary ventilation maneuvers performed on normal subjects have also shown a pressure pattern consistent with a predominant activity in expiratory abdominal muscles besides inspiratory chest wall and accessory muscles. The recruitment of the expiratory abdominal muscles has been suggested to result in unloading of the diaphragm during early inspiration when the abdominal muscles rapidly relax, permitting the gravitational forces to support the descent of the diaphragm. However, this breathing pattern was already seen in patient 1 and to a lesser extent in two patients (patients 4 and 5).

Increased use of the abdominal muscles has been observed in normal subjects during loaded breathing and in severely affected COPD patients at rest. The acceptance by some COPD patients of increased PCO$_2$ levels associated with high breathing frequencies and small Ti/Ttot ratios has been interpreted as a strategy to protect the respiratory muscles from fatigue.

According to our observations the diaphragm was far from the diaphragm-fatiguing levels defined in healthy subjects during loaded breathing. This might indicate that the weak diaphragm muscles in postpolio patients are more susceptible to fatigue and would explain the avoidance of a further increase in force at the cost of high PCO$_2$ levels. However, a contribution of eventual blunting of the chemoreceptors was not evaluated in the study.

The history of manifested respiratory failure in two of the five patients—patients 1 and 4—might be related to several factors. These two patients had the largest scoliotic angles. However, there was no consistent relation between scoliotic angles, vital capacity, A-a difference, and diaphragmatic force. This is in agreement with a study by Kafer, who found no significant correlations between scoliotic angles and vital capacity, blood gases, or A-a differences in patients with scoliosis caused by neuromuscular disorders. Patients 1 and 4 were the only patients with muscles strong enough to permit walking independently at relatively normal speeds. Thus, one might speculate that during daily life they exposed their respiratory muscles to a larger workload, causing intermittent blood gas impairment with a risk of desensitizing the responses to blood gas changes. These two patients also had sleep recordings showing hypoventilation.

In a study by Stanghelle and associates, it was suggested that the majority of the examined postpolio subjects had cardiorespiratory deconditioning and that exercise training would improve their physical performance. In contrast, four of our five patients had respiratory limitations for exercise and could come close to their limits during everyday life. One reason for the discrepancy could be that our patients were selected on the basis of severe respiratory muscle dysfunction. Another reason is that there might have been patients in the Stanghelle study whose respiratory limitation was not detected because arterial blood gases were not examined.

In conclusion, our study showed that in five postpolio patients with severe respiratory muscle dysfunction, breathing was the limiting factor for four of the patients and that the prevention of diaphragm fatigue at increased metabolic demands seems to be preserved at the cost of impaired blood gases. With respect to blood gases, the extent of respiratory dysfunction was not evident at rest, but was, however, revealed during the exercise test.

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Suppliers

a. Instrument Laboratories, Inc., Hartwell Avenue, PO Box 9113, Lexington, MA 02173-3190.

b. MGA 2000 Airspec; Centronic 20th Century Electronics Ltd, King Henry’s Drive, New Addington Croydon, CR9 0BG, United Kingdom.

c. Modified quadruple-lumen Swan Ganz Pacing-TD catheter, 93-2001-7F; Baxter Cardiovascular Group, 17221 Redhill Avenue, Irvine, CA 92614.

d. Erich Jaeger GmbH & Co., 97008 Wurtzburg, Germany.