Effects of an additional pressure support level on exercise duration in patients on prolonged mechanical ventilation

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exercise tolerance; pressure support ventilation; prolonged mechanical ventilation; pulmonary rehabilitation

Background/Purpose: Noninvasive positive pressure ventilation has been regarded as a strategy for improving exercise performance. Whether an increase in the ventilatory support level improves exercise performance in patients who have received invasive ventilation is unknown. The purpose of this study is to examine the effects of an additional level of pressure support (PS) ventilation on exercise tolerance in patients undergoing prolonged mechanical ventilation (PMV).

Methods: This study examined 15 patients who were undergoing PMV. All patients performed an upper-arm exercise test at three PS levels: the baseline PS level (PS), a level 2 cmH2O higher than the baseline level (PS+2), and a level 4 cmH2O higher than the baseline level (PS+4). The physiological response, reasons for discontinuing the exercise test, and exercise duration were recorded and analyzed.

Results: The tidal volume increased significantly from 271.7 ± 54.7 mL to 398.3 ± 88.7 mL at the PS+4 level (p = 0.01). Significant differences in exercise duration were observed at different PS levels. The exercise duration was significantly longer at the PS+4 level than at the PS and PS+2 levels (146.3 ± 139.9 seconds vs. 108.5 ± 85.9 seconds vs. 72.8 ± 43.9 seconds, p = 0.038) as their corresponding order. There were significant relationships between resting respiratory rate and exercise duration at the PS (r = −0.639, p = 0.034) and PS+2 levels (r = −0.668, p = 0.025).

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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Introduction

Patients with prolonged mechanical ventilation (PMV) have required at least 6 hours of mechanical ventilation for >21 consecutive days. Because of the advancement of critical care medicine, the number of patients dependent on PMV has rapidly increased worldwide. Studies have shown that 5–15% of patients with acute respiratory failure become reliant on PMV. Furthermore, 67% of patients undergoing PMV who were successfully weaned from a ventilator are readmitted within 3 months after discharge.

Patients undergoing PMV are commonly immobilized and experience complications of critical illness and mechanical ventilation, including muscle wasting and diaphragm dysfunction, that may adversely affect their functional statuses, ventilator weaning, and survival rates. Physical inactivity and deconditioning are common in mechanically ventilated patients with chronic respiratory failure. Scheinhorn et al reported that 98.7% of patients were bedridden at admission to post-intensive care unit (ICU) weaning centers and that 69% of patients were still bedridden at discharge from the weaning center. Even 12 months after discharge, only 19% of patients undergoing PMV can be fully active during daily life. All of the aforementioned complications may cause the mechanical ventilation dependency rates and hospitalization duration increase in patients undergoing PMV.

Pulmonary rehabilitation programs have proved to improve exercise tolerance and quality of life in patients with chronic respiratory disease. In one study, 85.6% of patients undergoing PMV were weaned from mechanical ventilators and were able to stand and ambulate after participating in a rehabilitation program. Exercise training has been regarded as the cornerstone of pulmonary rehabilitation. Most studies on exercise limitation and training have focused on spontaneously breathing patients with chronic obstructive pulmonary disease (COPD) because of the ventilatory and gas exchange impairment, along with the cardiac and skeletal muscle dysfunction that accompany this disease. However, few studies have investigated exercise response and strategies for improving training efficiency in patients with PMV.

The American Thoracic Society (ATS) suggested that high-intensity training produces substantial physiological benefits and exert positive training effects on exercise capacity and cardiopulmonary function, in patients with chronic respiratory diseases. However, high-intensity exercise is not always feasible in patients undergoing PMV, because they experience impaired pulmonary function and weak muscle. Applying additional noninvasive pressure ventilation (NIPPV) during exercise may enhance the exercise tolerance of unintubated patients with COPD, and enable these patients to achieve greater training intensity because it acutely reduces exertional dyspnea. Applying additional NIPPV is thus regarded as a strategy for improving exercise performance according to the ATS statement on pulmonary rehabilitation. Therefore, for intubated patients with severe cardiopulmonary impairment who are undergoing PMV, an increase in mechanical ventilatory support during exercise should improve exercise performance.

Pressure support ventilation (PSV) is a patient-triggered, pressure-limited, and flow-cycled mode of mechanical ventilation. When applied noninvasively to patients with COPD, PSV has been proven to consistently improve exercise endurance by reducing workload of breathing (WOB) during exercise. Whether an additional increase in the baseline pressure support (PS) level during exercise can improve exercise performance of patients undergoing PMV is unknown. Therefore, the purpose of the study is to compare the effects of three PS levels on the exercise tolerance and physiological response of patients undergoing PMV.

Methods

Patients

We enrolled patients from a respiratory care center at the Chang Gung Memorial Hospital, Tao-Yuan, Taiwan. After patients were medically stable and their mechanical ventilator settings were shifted from the assist-control mode to pressure-support mode, we evaluated their eligibility for the study. The inclusion criteria are listed as follows: (1) mechanical ventilation for >6 hours/day for >21 days and failure to be weaned from mechanical ventilation in ICUs; (2) alertness and ability to cooperate with the researchers; (3) medical stability [arterial blood gas value pH: 7.35–7.45, partial pressure of oxygen (PaO2): >60 mmHg at 40% fraction of inspiratory oxygen (FiO2), absence of signs and symptoms of infection, and hemodynamic stability]; and (4) mechanical ventilation by PS with a mechanical ventilation weaning program scheduled. Patients with cancer or neurological or other systemic diseases were excluded from the study. Patients unable to perform arm ergometry or to maintain an upright sitting position because of musculoskeletal problems, cardiovascular instability, or other conditions were also excluded. The study was conducted according to the principles established in the Declaration of Helsinki, and informed consent was obtained from the patients or their relatives before the patients participated in the study.

Study design

During the initial screening visit, patients’ medical histories, baseline weaning parameters [tidal volume (Vt),
respiratory rate (RR), minute volume (MV), maximal inspiratory pressure (Pimax), rapid shallow breathing index (RSBI)] and mechanical ventilator settings were recorded. All patients performed three exercise tests at three PS levels in a random sequence over 3 consecutive days. The three PS levels were defined as the baseline PS level (PS), a PS level 2 cmH2O higher than the baseline PS level (PS+2), and a PS level 4 cmH2O higher than the baseline PS level (PS+4). The baseline levels of positive end expiratory pressure (PEEP) and FiO2 were not changed throughout the study.

Endurance arm exercise test

The patients underwent an upper extremity ergometer test (Active Passive Train, Tzora Co, Kibbutz Tzora, Israel) in an upright position in their beds. All patients were familiarized with the cycling equipment prior to participating in the study. The exercise test protocol was selected according to the method described by van’t Hul et al. Patients underwent a constant-load, symptom-limited exercise test at fixed resistance (approximately 10 W) in each test. They were encouraged to perform the exercise to the point of intolerable shortness of breath, discomfort, or exhaustion. On the basis of the American College of Chest Physicians (ACCP) guidelines on cardiopulmonary exercise testing, the test was terminated if one of the following conditions was observed: (1) heart rate (HR) > 80% of the age-predicted maximal HR; (2) systolic blood pressure (BP) ≥ 220 mmHg, or diastolic BP ≥ 120 mmHg; (3) a decrease in BP ≥ 10 mmHg compared with the resting status; (4) abnormalities such as ventricular tachycardia, ventricular premature contraction, atrioventricular block, or ventricular flutter were observed on an electrocardiogram; (5) severe angina; (6) signs of poor perfusion, or SpO2 ≤ 90% or ≥ 5% decrease in saturation of peripheral oxygen (SpO2); (7) symptoms related to the nervous system such as ataxia, dizziness, or confusion; (8) the patient requested to stop; or (9) the patient reported fatigue or shortness of breath (Borg scale > 5), wheezing, or arm cramps. During each exercise test, vital signs and electrocardiogram were continually monitored using a bedside computerized monitoring system (Philips Medizin System GmbH 71034, Böblingen, Germany) to evaluate the exercise response of the patients. We recorded the total exercise duration and physiological responses, including the HR, RR, BP, and SpO2, as well as the reasons for discontinuing exercise during each exercise test.

Statistical analysis

Data were analyzed using the SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL, USA). Prior to all analyses, the one-sample Kolmogorov–Smirnov test was used to determine the normality of the data. The results were expressed as the mean ± standard deviation for nominal distributions, and as median and interquartile range for nonparametric distributions.

To examine the effects of respiratory muscle strength on exercise duration, study participants were divided into two groups: high Pimax group: Pimax < –30 cmH2O (n = 9); and low Pimax group: Pimax > –30 cmH2O (n = 6). A two-way analysis of variance analysis was used to examine the differences among conditions (PS, PS+2, and PS+4) and between groups. Pearson correlation coefficients between the exercise endurance and weaning parameters were calculated. A stepwise regression analysis was used to determine factors that contribute to the improvement of exercise endurance. A p value < 0.05 indicated statistical significance.

Results

Patient characteristics

The demographic and clinical characteristics of the patients are presented in Table 1. Fifteen patients were recruited and completed all exercise tests at the three PS levels. The mean age of the patients was 73.1 ± 11.2 years, and the majority of patients were women (73%). Congestive heart failure was diagnosed in approximately half of the patients. Table 2 shows the weaning parameters and arterial blood gas values of patients. Most of the patients exhibited low Vt and hypercapnia prior to participating in the study.

Physiological response during exercise tests at various PS levels

Table 3 shows the physiological responses at the three PS levels. The baseline PS level was 10.7 ± 3 cmH2O. As the PS level increased from baseline to PS+4 levels, the Vt significantly increased from 271.7 ± 54.7 mL to 398.3 ± 88.7 mL (p = 0.001). Moreover, patients exhibited significantly higher MV at the PS+4 level than at the PS level (7.8 ± 2.2 L vs. 6.2 ± 1.4 L, p = 0.041). No differences were observed in the RR, SpO2, and HR at rest among the three PS levels. All patients completed the exercise at peak volitional exertion at each level. Table 4 lists the reasons for discontinuing exercise during each test. No significant differences among the three PS levels in the changes of vital signs at the end of the exercise test were observed. Most exercise tests discontinued for more than one reason. Shortness of breath was the most common reason for discontinuing the exercise test at all PS levels.

Effects of additional PS on exercise performance

Fig. 1 shows the exercise performance according to the PS level. Significant differences in exercise duration among the three PS levels were observed. The exercise duration was significantly longer at the PS+4 level compared with the baseline PS level (146.3 ± 139.9 seconds vs. 108.5 ± 85.9 seconds vs. 72.8 ± 43.9 seconds, p = 0.038). Compared with exercise endurance at the PS level, exercise endurance was greater in nine patients (60%) at PS+2 and in 14 patients (93%) at PS+4. The percentage of improvement in exercise endurance was 16% (~ 13.6 to 129.7%) at the PS+2 level and 36% (8.4–101.6%) at the PS+4 level.

Fig. 2 shows a comparison of exercise duration between the low and high Pimax groups. The high Pimax group could
exercise for a longer period than the low Pimax group could at the three PS levels. However, the differences were not statistically significant. In the low Pimax group, the patients exercised significantly longer at the PS level\(^+4\) level than the PS level [66.0 (40.6–106.0) seconds vs. 42.0 (32.5–76.0) seconds, \(p = 0.043\)]. No significant differences were observed among the three PS levels in the high Pimax group [PS vs. PS\(^+2\) vs. PS\(^+4\): 88.0 (62.5–135.3) seconds vs. 77.5 (47–138.5) seconds vs. 93.0 (56.5–214.0) seconds, \(p = 0.247\)].

Among the weaning parameters, significant correlations were observed between the RR and exercise duration at the PS (\(r = 0.639, p = 0.034\)) and PS\(^+2\) levels (\(r = 0.668, p = 0.025\)). No significant correlation was observed between vital sign changes and exercise duration at the three PS levels. Significant correlations were also observed between improvement of exercise endurance at PS\(^+2\) levels and age (\(r = 0.650, p = 0.02\)), and between improvement of exercise endurance at PS\(^+2\) levels and PaO\(_2\) (\(r = 0.630, p = 0.02\)). No statistically significant correlation coefficients were observed between improvement of exercise endurance at PS\(^+4\) levels and weaning parameters, nor arterial blood gas data. In a stepwise multiple regression analysis, age and PaO\(_2\) jointly significantly contributed to improvement of exercise endurance when the PS\(^+2\) levels was applied during exercise explaining 68.3% of the variance in the outcome (\(p = 0.02\)).

### Discussion

To our knowledge, this is the first study to investigate the effect of additional PS levels on exercise tolerance in patients on PMV. In our study, the Vt increased significantly when the PS level was increased. The patients exhibited significantly longer exercise durations when they exercised at the PS\(^+4\) level.

The PS mode is often used for weaning in an ICU. At low levels of support, this mode unloads the WOB that the ventilator tubing imposes on the respiratory muscles. At high levels of support, the ventilator can reduce respiratory...
In our study, exercise duration was significantly greater at the PS + 4 level than at the PS level, especially in the low Pimax group. The impaired respiratory muscle strength has been reported as one of the reasons for exercise intolerance in patients with chronic lung disease. During exercise, the increased ventilatory demand may cause diaphragm ischemia, thus inducing muscle metaboreflex and a subsequent sympathetic-mediated vasoconstriction in the exercising peripheral muscles. Exercise of peripheral muscle groups results in a quick rise in plasma lactate, which further increased ventilatory load on respiratory muscle and results in poor exercise tolerance. The results of the current study confirm those of previous studies in which patients exercise with PSV level at their baseline PS level (PS); PS + 2 = patients exercise with PS level at 2 cmH2O greater than their baseline PS level; PS + 4 = patients exercise with PS level at 4 cmH2O higher than their baseline PS level; RR = respiratory rate; SpO2 = saturation of peripheral oxygen; Vt = tidal volume.

Table 3 Resting physiologic variables under different pressure support levels in patients on prolonged mechanical ventilation.

<table>
<thead>
<tr>
<th></th>
<th>PS</th>
<th>PS + 2</th>
<th>PS + 4</th>
<th>p</th>
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<tbody>
<tr>
<td>Vt (mL)</td>
<td>271.7 ± 54.7</td>
<td>313.0 ± 62.0</td>
<td>398.3 ± 88.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>RR (bpm)</td>
<td>22.8 ± 2.0</td>
<td>18.9 ± 4.39</td>
<td>19.1 ± 4.2</td>
<td>0.115</td>
</tr>
<tr>
<td>MV (L)</td>
<td>6.2 ± 1.4</td>
<td>5.9 ± 1.7</td>
<td>7.8 ± 2.2</td>
<td>0.041</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>83.0 ± 13.9</td>
<td>82.1 ± 16.7</td>
<td>83.9 ± 12.8</td>
<td>0.396</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>98.6 ± 11.8</td>
<td>99.1 ± 14.6</td>
<td>93.6 ± 17.0</td>
<td>0.163</td>
</tr>
<tr>
<td>SpO2 (%)</td>
<td>96.6 ± 1.7</td>
<td>96.0 ± 2.2</td>
<td>97.3 ± 2.2</td>
<td>0.311</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation.

HR = heart rate; MV = minute volume; PS = patients exercise with PSV level at their baseline PS level (PS); PS + 2 = patients exercise with PS level at 2 cmH2O greater than their baseline PS level; PS + 4 = patients exercise with PS level at 4 cmH2O higher than their baseline PS level; RR = respiratory rate; SpO2 = saturation of peripheral oxygen; Vt = tidal volume.

Table 4 Peak exercise responses under different pressure support levels in patients on prolonged mechanical ventilation.

<table>
<thead>
<tr>
<th></th>
<th>PS</th>
<th>PS + 2</th>
<th>PS + 4</th>
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<tbody>
<tr>
<td>PS level (cmH2O)</td>
<td>10.7 ± 3</td>
<td>12.8 ± 2.8</td>
<td>13.6 ± 2.6</td>
</tr>
<tr>
<td>Peak HR (bpm)</td>
<td>93.8 ± 18.9</td>
<td>91.0 ± 14.3</td>
<td>89.3 ± 13.5</td>
</tr>
<tr>
<td>Peak HR (% of predicted values)</td>
<td>63.9 ± 11.5</td>
<td>62.1 ± 8.1</td>
<td>60.8 ± 8.7</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>93.8 ± 12.1</td>
<td>95.3 ± 12.9</td>
<td>92.8 ± 10.3</td>
</tr>
<tr>
<td>SpO2 (%)</td>
<td>96.9 ± 2.7</td>
<td>96.7 ± 2.4</td>
<td>96.5 ± 1.9</td>
</tr>
<tr>
<td>RR (bpm)</td>
<td>27.3 ± 6.8</td>
<td>27.3 ± 9.1</td>
<td>25.9 ± 9.4</td>
</tr>
</tbody>
</table>

Reasons for stopping exercise:

- Arrhythmia: 1/15 (6.7%)
- SpO2 drop: 1/15 (6.7%)
- Shortness of breath: 13/15 (86.7%)
- Exhaustion: 9/15 (60%)
- Muscle soreness/weakness: 2/15 (13.4%)

Data are presented as mean ± standard deviation.

HR = heart rate; PS = patients exercise with PSV level at their baseline PS level (PS); PS + 2 = patients exercise with PS level at 2 cmH2O greater than their baseline PS level; PS + 4 = patients exercise with PS level at 4 cmH2O higher than their baseline PS level; RR = respiratory rate; SpO2 = saturation of peripheral oxygen.
COPD who received a high level of PS exhibited higher ox-level (PS); PS pressure support ventilation (PSV) level at their baseline PS previous study. Vitacca et al reported that patients with the positive effect of additional ventilatory support on Z with greater improvement in exercise duration at the PS Patients who exhibited lower resting PaO2 were associated the improvement of exercise duration at the PS

Figure 1 Effects of different pressure support level on exercise duration in patients on prolonged mechanical ventilation. *p < 0.05, comparison between PS and PS+4 levels. PS (pressure support) = patients exercise with pressure support ventilation (PSV) level at their baseline PS level (PS); PS+2 = patients exercise with PS level at 2 cmH2O greater than their baseline PS level; PS+4 = patients exercise with PS level at 4 cmH2O higher than their baseline PS level.

observed in the current study indicates that applying additional PS during exercise may be a strategy for improving efficiency of exercise training in patients undergoing PMV.

In our study, age and PaO2 level significantly contributed the improvement of exercise duration at the PS+2 levels. Patients who exhibited lower resting PaO2 were associated with greater improvement in exercise duration at the PS+2 levels (r = −0.630, p = 0.02), indicating an association between the impaired ventilatory capacity of patients and the positive effect of additional ventilatory support on exercise ability. This result was consistent with that of a previous study. Vitacca et al reported that patients with COPD who received a high level of PS exhibited higher oxygen saturation during exercise compared with status

Figure 2 Exercise endurance of low and high maximal inspiratory pressure (Pimax) group under different PS levels. *p < 0.05, comparison between PS and PS+4 levels in low Pimax group. PS (pressure support) = patients exercise with pressure support ventilation (PSV) level at their baseline PS level (PS); PS+2 = patients exercise with PS level at 2 cmH2O greater than their baseline PS level; PS+4 = patients exercise with PS level at 4 cmH2O higher than their baseline PS level.

without PS. Patients who exhibited lower PaO2 at rest have a higher risk of being hypoxemic during exercise because of their impaired oxygenation status. The additional ventilatory support may improve alveolar ventilation by increasing the Vt and reducing the RR during exercise, thus prolonging exercise duration.

We adjust the PS level in increments of 2 cmH2O according to the protocol of Chao et al. They developed a weaning protocol for patients in a respiratory care center and increased or reduced the PS levels by 2 cmH2O depending on whether patients tolerated the current status well or not for >24 hours. Therefore, we used 2 cmH2O as an increment in each session. In addition, it has been reported that an excessive PS level increases the risk of hyperinflation and discomfort in patients. Thus, we used the level up to 4 cmH2O as the upper limit.

Limitations

Our study has several limitations. Although the number of patients in this study was comparable with that of previous studies that yield with positive results, we are aware that the small sample size may hamper interpretation of the results. Additional studies with larger sample sizes are required. Second, previous studies have reported that additional NIPPV support may unload respiratory muscles, improve peripheral muscle oxygenation, and reduce blood lactate levels, thus reducing dyspnea. Our patients exhibited a similar level of dyspnea but a prolonged exercise duration at PS+4 level. However, because of equipment and technical limitations, we were unable to obtain data on respiratory muscle activity and blood lactate levels, which should be obtained in future studies. The third limitation was the differences in diagnoses among the patients. Congestive heart failure was diagnosed in almost half of our patients (46.7%). A study has reported that the effect of positive pressure varies between cardiac and pulmonary diseases. Variations in underlying pathological conditions of patients may partly explain the variations in exercise duration. The last limitation is that although we observed a significant improvement of exercise duration with PS+4 levels, whether a higher PS level would induced longer exercise duration in patients on PMV remain questionable. Medadue et al reported that the exercise duration as significantly longer at PS level of 20 cmH2O than at sham PS level in patients with COPD, which is higher than the mean value of PS+4 group (13.6 cmH2O) in our study. Because the degree of reduction on work of breathing is related to the level of ventilator support, the PS+4 level in our study may be not the optimal level for patients undergoing PMV. Further studies are needed to confirm the optimal support level for patients undergoing PMV to improve exercise performance.

Our study demonstrated that an increased PS level is associated with a longer exercise duration compared with the baseline PS level, especially in patients undergoing PMV with low respiratory muscle strength (Pimax ≥ 30 cmH2O) and rapid breath at rest. This beneficial effect might result from an increase in the Vt, which is produced by an increased PS level. In patients undergoing PMV who have engaged in exercise, applying additional ventilatory
support produces an immediate improvement in exercise duration and may confer a training advantage. However, additional studies are required to determine this mechanism.

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