Esophageal-Directed Pressure Support Ventilation in Normal Volunteers*

Mathew Barnard, MBBS; Avinash Shukla, MBBS; Tim Lovell, MBBS; and John Goldstone, MBBS

Study objectives: To ascertain whether inspiratory pressure support (IPS) can be triggered reliably from and targeted at esophageal pressures (Pes), and to compare the work of breathing and time delay to initiation of inspiratory flow between conventional pressure support and esophageal-directed pressure support (EDPS).

Design: Prospective laboratory study.

Setting: University medical school.

Patients or participants: Five normal volunteers.

Interventions: IPS at a level to achieve tidal volume of 10 mL/kg, and EDPS with a target Pes of 0 cm H2O via full facemask.

Measurements and results: Pes, airway pressure, and inspiratory flow were measured during spontaneous breathing. Peak Pes and pressure time product (PTP) of Pes were calculated during spontaneous breathing and through linear resistances. Measurements were repeated during IPS and EDPS ventilation. At rest, PTP was 7.56 (± 3.6) and peak Pes was −5.8 cm H2O (± 1.44). When subjects were breathing through the resistors, PTP increased to 12.4 (± 8.1) and 30.3 (± 5.9) and peak Pes decreased to −7.2 and −15.3 cm H2O respectively. With facemask IPS, unloaded PTP fell to 1.7 (± 1.3) and peak Pes fell to −3.3 cm H2O (± 1.3). When ventilated through the highest resistance with IPS, mean PTP increased to 21.9 and peak Pes increased to −11.9 (± 4.2) cm H2O relative to baseline. During EDPS with the resistor, PTP fell to 1.5 ± 1.1 (p < 0.007) and peak Pes fell to −1.9 ± 1.1 cm H2O (p < 0.0001).

Conclusions: It was possible to initiate supported breathing from Pes values. The work performed, as measured by PTP, was lower during EDPS than during either unsupported breathing or conventional IPS. (CHEST 1999; 115:482–489)

Key words: esophageal pressure; mechanical ventilation; triggering of ventilation

Abbreviations: EDPS = esophageal-directed pressure support; IPS = inspiratory pressure support; PEEP = positive end-expiratory pressure; Pes = esophageal pressure; PTP = pressure time product

Mechanical ventilation comprises a number of modes, many of which allow spontaneous breathing. Since the early 1970s, increasingly sophisticated methods have been devised to make the interaction between the patient and the ventilator as sensitive as possible. To reduce the work performed during the initial phase of inspiration, a demand valve opens rapidly in response to a change in either airway pressure or flow. Inspiratory pressure support (IPS) is a mode of ventilation that characteristically generates a constant target pressure within the airway with high initial inspiratory flow rates until a target pressure is reached. IPS is initiated by the patient, the target pressure is preset, and inspiratory work can be adjusted by altering the preset target pressure.1

The provision of ventilatory support for the patient is dependent on the ability of the ventilator to sense inspiration. Furthermore, airway pressure must be transmitted to the chest effectively such that alveolar pressure is positive during inspiration. Under ideal circumstances, the ventilator senses inspiration immediately and little pressure difference occurs across the lungs. This is usually achieved in normal subjects or patients with normal lung mechanics with the result that inspiratory work during mechanical ventilation can be reduced by ≥ 70%.

When lung mechanics are abnormal, many factors prevent rapid detection of inspiration by the ventilator, the essential element being that transmission of the inspiratory signal to the ventilator is delayed.

*From the Department of Anaesthesia, University College London Medical School, London, UK.

Manuscript received January 28, 1998; revision accepted September 3, 1998.

Correspondence to: John Goldstone, Department of Anaesthesia, University College London Medical School, Room 103, The Middlesex Hospital, Mortimer Street, London W1N 8AA, United Kingdom; e-mail j.goldstone@ucl.ac.uk

482 Clinical Investigations in Critical Care
In addition, the preset pressure may be dissipated across the lungs and without measurement of alveolar pressure, the patient may be performing inspiratory work at levels equivalent to unassisted breathing. The inspiratory work performed by the patient is often not recognized and described at the bedside as the patient “fighting the ventilator.” In this circumstance, there is a substantial amount of energy wasted resulting in patient discomfort.

It would be preferable to trigger the ventilator from a more direct indicator of inspiratory muscle contraction. The effect of the site of the inspiratory trigger on the patient-ventilator interface was investigated in a mechanical lung model by Takahashi and coworkers. They found that triggering inspiratory pressure assistance from the esophageal pressure (Pes) deflection always reduced the work performed when compared with conventional IPS. While conventional ventilation only lowered inspiratory work to baseline unloaded levels in the presence of simulated lung disease, esophageal triggering was associated with inspiratory work of < 10% of baseline.

We aimed to investigate whether this was a potential strategy in humans. Supplying the ventilator with pressure signals from the esophagus implies that supported breaths are both triggered from and targeted at pleural pressure (as reflected by Pes). Thus, the work of the triggering component ought to be minimized owing to early transmission of the pressure change signal to the ventilator, and the target pressure ought to be directly related to the ventilatory workload. A discrepancy between the frequency of inspiratory muscle efforts and the frequency of supported breaths has been described as dysynchrony. This may arise due to a difference between the pleural pressure reduction produced by the inspiratory muscles and the sum of intrinsic positive end-expiratory pressure (PEEP) plus trigger pressure. Triggering the inspiratory pressure assistance from the esophagus removes the requirement to overcome intrinsic PEEP before the trigger threshold is achieved. This could reduce the possibility of ineffective respiratory efforts and hence dysynchrony. Additionally targeting the muscle effort may more closely match ventilatory flow to requirements, and thus minimize excessive pressure or volume assistance. This in turn might reduce the incidence of intrinsic PEEP. Finally, the use of an earlier signal than is conventionally used could decrease the response time to initiation of gas flow, and potentially enhance patient-ventilator interaction and patient comfort. We have termed this mode esophageal directed pressure support (EDPS). We set out to investigate the feasibility and practicality of EDPS in human volunteers and measure the work of breathing and degree of patient ventilator desynchrony when compared with conventional IPS.

**Materials and Methods**

Five normal human volunteers were studied after providing informed consent to a protocol approved by the institutional review committee. All were nonsmokers with a body mass index < 25, who had no intercurrent disease.

Subjects breathed through a ventilator (Servo 900C; Siemens; Berkshire, UK) in pressure support mode. Flow and airway pressure were measured at the circuit-Y. Inspiratory and expiratory pressure-sensing transducers inside the ventilator were connected together with plastic tubing and joined by a three-way tap to the esophageal balloon catheter. Another three-way connection allowed the Pes signal to be simultaneously monitored on the recording instruments.

**Measurements**

Airway pressure, Pes, and inspiratory flow rate were measured for each subject. Airflow was measured with a heated pneumotachograph (Hans Rudolph; Kansas City, MO) and volume was obtained from the integrated flow signal. A tight-fitting sealed face mask was strapped to each subject and tested to be leak free at 35 cm H2O. The pneumotachograph and airway pressure transducer were placed between the face mask and “Y” of the ventilator tubing. Pes was measured using a 10-cm latex balloon catheter filled with 0.5 mL of air (P.K. Morgan; Kent, UK). Appropriate placement of the balloon was according to the method described by Baydur et al. Pressure and flow were calibrated with a water manometer and an air flowmeter (Platon; London, UK).

All measurements were received by a signal processing box (Precision Medical Ltd; Northampton, PA) and then recorded on a microprocessor system (Apple Macintosh; Cupertino, CA). The signals were recorded, stored, and analyzed using virtual instruments developed within a software package (Lab View 2.2; National Instruments; Austin, TX).

All subjects were trained in breathing investigations and were seated upright. Breaths were timed at 10/min with a metronome timer. Subjects monitored tidal volume as they breathed with a target of 10 mL/kg in each breath. Respiratory disease was simulated with added resistances. Resistive breathing was achieved with linear 5-mm and 3-mm diameter resistors added to the ventilator circuit.

The ventilator controls were adjusted to enable sensing from Pes. In some subjects, resting Pes at the end of expiration was above zero. This was misinterpreted by the ventilator as a positive airway pressure when configured in EDPS mode. To avoid an increased load, whereby the negative deflection in Pes to successfully trigger the ventilator would have to equal the resting end expiratory Pes plus the triggering pressure, PEEP was applied. Since the ventilator is designed to trigger when airway pressure falls to a set level below PEEP, triggering during EDPS then occurred when Pes was equal to PEEP (which was equal to resting Pes) minus the triggering pressure.

**Protocol**

Subjects breathed at rest without the ventilator for baseline measurements. The subjects then breathed through the ventilator in pressure support mode. The pressure support level was adjusted to produce a tidal volume of 10 mL/kg. Measurements
were taken with the subjects breathing through no additional resistance. Measurements were then repeated with the 5-mm and 3-mm resistance connectors. EDPS ventilation was instituted and measurements were taken at a target Peso level of 0 cm H2O. The working pressure of the ventilator was adjusted until a target tidal volume of 10 mL/kg was achieved. Measurements were repeated in EDPS mode when breathing through 5-mm and 3-mm resistances.

Data Analysis

All measurements were analyzed using custom virtual instruments in the software package (Labview 2.2). The pressure time product (PTP) of the inspiratory esophageal waveform was calculated as the integral of Peso with regard to time during inspiration from the beginning of patient effort indicated by the fall in Peso, to return to baseline.6 The inspiratory response delay was taken as the time between the first negative Peso deflection and the initiation of inspiratory flow from the ventilator. Inspiratory response delays were measured for unloaded and 3-mm resistive breathing during IPS and EDPS. The duration of inspiration was directly measured from the beginning to the end of flow. The maximal negative Peso was measured from the pressure tracings.

The mean of five representative breaths from each ventilator setting was used for analysis. Differences between IPS and EDPS were evaluated during each breathing condition using the paired t test as modified by Dunnett. Values obtained under the two different ventilatory modes and resistances were assessed using two-way analysis of variance. Significance was taken as a p value of <0.05.

Results

In all subjects, the inspiratory time delay was reduced during EDPS compared with IPS. The reduction in time delay ranged from 4 to 55%. During IPS, mean time delay was 310 ms (± 50) unloaded and 350 ms (± 90) with the 3-mm resistance. During EDPS, mean time delay was significantly reduced when unloaded (170 ± 40 ms, p < 0.001) or loaded with the 3-mm resistance (180 ± 50 ms, p < 007, Table 1). Figure 1 demonstrates individual time delay results in five subjects breathing with and without the 3-mm inspiratory resistance for both modes of ventilation.

During spontaneous breathing, mean PTP was 7.56 (± 3.6). During pressure support ventilation, mean PTP fell significantly (1.72 ± 1.2, p < 0.009). During EDPS, mean PTP was significantly lower than during spontaneous breathing or during IPS ventilation (PTP, 0.46 ± 0.23, p < 0.001, Table 2).

With the addition of the 5-mm resistance, mean PTP during spontaneous ventilation increased to 12.4 (± 8.1). With IPS, PTP fell (3.62 ± 2.4) and with EDPS ventilation mean PTP declined further (0.60 ± 0.25). PTP was significantly less during EDPS compared with IPS or with spontaneous breathing (p < 0.01).

At the highest resistance (3 mm) during spontaneous breathing, mean PTP rose to 30.3 (± 8.32), a fourfold increase from unloaded, and was noticed as an increase in the inspiratory work by all subjects. With IPS, mean PTP fell to 21.8 (± 15.1) whereas with EDPS mean PTP fell significantly when compared with spontaneous breathing or IPS (1.14 ± 1.1, p < 0.01, Fig 2).

The peak esophageal negative pressure during spontaneous breathing was -5.8 cm H2O and this decreased to -15.3 cm H2O at the highest level of inspiratory resistance (Fig 3). With the 3-mm resistance peak negative pressure increased during IPS ventilation (-11.96 cm H2O) but it was not possible to achieve an inspiratory negative pressure above baseline values (p = 0.24). EDPS increased peak inspiratory pressure to the same level as baseline with or without the resistances and was significantly different from spontaneous breathing or IPS (p < 0.0009, Table 3).

Discussion

Mechanical ventilation is widely used in patients as it allows respiratory muscle rest and control of arterial blood gases. Since the 1970s, controlled ventilation has been followed or replaced by modes of assisted spontaneous ventilation, in which the philosophy is to divide the respiratory load between the patient and the machine. In theory, the clinician chooses the proportions borne by the patient or machine according to individual patient considerations. However, early efforts at allowing patients to breathe through ventilator circuitry were hampered by apparatus-imposed additional work loads due to unsophisticated valve technology. Advances in ventilator design have greatly reduced their resistance to spontaneous breathing and once again assisted or supported ventilation is widely practiced. IPS is a popular mode and may be the method of choice in managing the transition from mechanical ventilation to spontaneous breathing.6,7 However, there remains

---

Table 1—Inspired Time Delay Recorded in Five Normal Subjects Breathing Through the Ventilator With Conventional IPS or From EDPS

<table>
<thead>
<tr>
<th></th>
<th>Loaded (3 mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unloaded</td>
</tr>
<tr>
<td>Mean inspiratory time delay (ms)</td>
<td>0.31</td>
</tr>
<tr>
<td>SD</td>
<td>0.05</td>
</tr>
<tr>
<td>Mean inspiratory time delay (ms)</td>
<td>0.17</td>
</tr>
<tr>
<td>SD</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Clinical Investigations in Critical Care
a requirement for improving the patient ventilator interaction, particularly in patients with increased airway resistance.

EDPS involves triggering the ventilator from an earlier signal of inspiratory effort than the conventionally used airway pressure. This carries three potential advantages. The first reflects the fact that in order to decrease airway pressure, a reduction in pleural pressure must be transmitted across the airways to the site of pressure measurement. In the presence of significant lung disease, the work performed by the respiratory muscles in reducing airway pressure to the trigger threshold may be substantial.8,9 EDPS obviates the need for transmission of the pressure drop to the airway opening, and hence might decrease that part of the work of breathing which is associated with triggering the ventilator. This is not only of theoretical concern. The endotracheal tube and apparatus can increase the work of breathing substantially.10–12 Bersten et al13 demon-

Table 2—PTP Recorded in Five Normal Subjects Breathing Through the Ventilator With IPS or From EDPS

<table>
<thead>
<tr>
<th></th>
<th>Unloaded</th>
<th>5 mm</th>
<th>3 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean PTP during spontaneous ventilation</td>
<td>7.56</td>
<td>12.48</td>
<td>30.38</td>
</tr>
<tr>
<td>SD</td>
<td>3.64</td>
<td>8.12</td>
<td>8.93</td>
</tr>
<tr>
<td>Mean PTP during IPS</td>
<td>1.72</td>
<td>3.62</td>
<td>21.88</td>
</tr>
<tr>
<td>SD</td>
<td>1.28</td>
<td>3.45</td>
<td>19.32</td>
</tr>
<tr>
<td>Mean PTP during EDPS</td>
<td>0.46</td>
<td>0.60</td>
<td>1.48</td>
</tr>
<tr>
<td>SD</td>
<td>0.23</td>
<td>0.25</td>
<td>1.10</td>
</tr>
</tbody>
</table>
strated that certain configuration of circuits plus endotracheal tubes imposed a level of work high enough to require mechanical ventilation.

The second advantage of an earlier signal of inspiratory effort is a potential reduction in failing to trigger the ventilator. Dysynchrony describes a discrepancy between the frequency of inspiratory efforts and the frequency of supported breaths. This discrepancy arises because a difference may develop between the negative pressure generated by the contracting inspiratory muscles and excessive elastic recoil of the respiratory system. This situation is particularly likely to arise in the presence of increased flow resistance and significant intrinsic PEEP. Respiratory muscle efforts must be greater than the sum of intrinsic PEEP plus trigger pressure to successfully trigger the ventilator. In the setting of significant intrinsic PEEP, the magnitude of pressure developed by the respiratory muscles can be substantial. This not only increases the work of breathing associated with triggering as above, but implies that contractions smaller than this amount will fail to trigger the ventilator. These ineffective efforts may be uncomfortable, and also carry a metabolic cost. EDPS takes Pes as a baseline and allows triggering when Pes falls only by the triggering pressure—without the need to additionally overcome the magnitude of intrinsic PEEP. It is thus possible that in situations in which ineffective inspiratory efforts are occurring, the frequency of these will decline. Since this situation may not be detected clinically, this is of additional benefit.

A further advantage of EDPS is that inspiratory pressure assistance is targeted at a signal that closely

![Figure 2. PTP of Pes per breath measured during spontaneous breathing, IPS, and EDPS. Subjects were breathing (top, a) unloaded or (bottom, b) through an inspiratory resistance.](http://publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21906/)
represents muscle effort. Assessing the optimal level of pressure support for an individual patient is difficult and currently engenders as much debate as determining the optimal PEEP once did.\textsuperscript{14} A variety of methods have been suggested, including diaphragm electrical activity.\textsuperscript{15} Insufficient pressure support will not sufficiently decrease the ventilatory workload, potentially causing fatigue, while excessive pressure support implies totally unloading the respiratory muscles for too long a period of time. This could result in muscle disuse and atrophy. Since EDPS seeks to maintain Pes at zero, as patient effort increases, so will the delivered flow and pressure. If Pes is actually maintained at zero, any inspiratory muscle effort acting to decrease Pes should be rewarded with an exact amount of gas flow that changes Pes by an amount equal and opposite to that produced by the muscle activity.

This study reinforces the concepts proposed by Banner et al\textsuperscript{16} who have also investigated the impact of moving the inspiratory trigger distal to the airway opening. They concluded that by measuring pressure at the distal end of the endotracheal tube, pressure support can compensate appropriately for work imposed by breathing apparatus. This work also underlines the importance of taking into account the resistance and imposed work of the endotracheal tube and airways. Previous improvements to the patient ventilator interaction, such as flow triggering, have concentrated on measurements taken from and interventions directed at circuit pressures.\textsuperscript{17} However the documented advantages of flow triggering...

---

**Figure 3.** Peak inspiratory Pes measured during spontaneous breathing, IPS, and EDPS. Subjects were breathing (top, a) unloaded or (bottom, b) through an inspiratory resistance.
Our results confirm that it is possible to initiate assisted ventilation from esophageal waveforms. Furthermore, when pleural pressure is targeted, inspiratory work is substantially less than that seen with conventional pressure support ventilation. When inspiratory resistance is high, the effect of triggering and targeting Pes is more pronounced. It was also possible to ventilate normal subjects from a standard esophageal balloon catheter by simply connecting it to the inspiratory pressure transducer of the ventilator. The inspiratory pressure transducer is readily accessible in the ventilator (Servo 900C) and inspiratory flow is switched on when inspiratory pressure is below the trigger set by the user. Although our simple system requires modification to overcome the inhibitory effects of esophageal contraction, suitable algorithms could be developed to overcome this problem.

EDPS is a novel method of triggering mechanical ventilation that we have applied successfully to normal subjects. EDPS substantially reduces inspiratory work in the face of changing inspiratory resistance, and this would occur on a breath-by-breath basis without the need for recognition by the clinician of the level of mechanical work appropriate to the subject. A major limitation of this study is that subjects were volunteers, with simulated increases in airway resistance. It is not possible to exactly and reliably mimic with normal volunteers the physiologic challenges posed by patients with advanced COPD. We believe that our findings suggest that future work aimed at assessing the potential for providing inspiratory assistance with EDPS to intubated patients with airway disease would be valuable.

Table 3—Peak Negative Esophageal Inspiratory Pressure in Five Normal Subjects During Spontaneous Ventilation, IPS, and EDPS

<table>
<thead>
<tr>
<th></th>
<th>Unloaded</th>
<th>5 mm</th>
<th>3 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean peak negative pressure during SV (cm H₂O)</td>
<td>−5.54</td>
<td>−7.2</td>
<td>−15.34</td>
</tr>
<tr>
<td>SD</td>
<td>1.44</td>
<td>0.69</td>
<td>4.17</td>
</tr>
<tr>
<td>Mean peak negative pressure during IPS</td>
<td>−3.32</td>
<td>−3.06</td>
<td>−11.96</td>
</tr>
<tr>
<td>SD</td>
<td>1.37</td>
<td>1.24</td>
<td>4.20</td>
</tr>
<tr>
<td>Mean peak negative pressure during EDPS</td>
<td>−1.38</td>
<td>−1.52</td>
<td>−1.94</td>
</tr>
<tr>
<td>SD</td>
<td>0.68</td>
<td>0.61</td>
<td>1.14</td>
</tr>
</tbody>
</table>

Our results confirm the work of breathing imposed by the endotracheal tube. Although flow triggering is statistically superior to conventional pressure triggering, the difference might not be statistically significant. The difference between flow triggering and tracheal triggering is substantial compared with the difference between flow and pressure triggering. Similarly the inspiratory work of breathing in our study with esophageal triggering is many times smaller than IPS, and the difference between the two is likely to be very much greater than any difference between conventional flow and pressure triggering. We have simply taken the work of Banner et al one step further by siting pressure measurement in the esophagus. This allows for adjustment of pressure support to pleural deflection, which compensates for pulmonary mechanics. In the same way that moving the pressure measuring site to the trachea obviates the patient from overcoming the resistance of the endotracheal tube to initiate flow, moving the site to the pleura removes the need to overcome the resistance of the distal airway. This might be particularly relevant in the setting of high airway resistance, when the work required to trigger gas delivery approaches critical levels.

The reduction in work of breathing associated with EDPS was substantial. Mean PTP fell by 80% when normal subjects were ventilated with IPS, but fell much further with EDPS, and it was possible to almost abolish inspiratory work in all subjects. At high levels of inspiratory resistance, PTP increased by up to sixfold when breathing without assistance. With the highest resistance, IPS was unable to reduce inspiratory effort to levels of unloaded unassisted breathing. By contrast, EDPS resulted in PTP levels that were a fraction of their loaded level. During EDPS, PTP was reduced to <2% of loaded PTP, and in all subjects, PTP was <20% of the unloaded unassisted PTP values. These substantial differences augur well for potential future clinical applications of this technique.

References