Pressure-support ventilation and diaphragm shortening in the rat model

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Anesthesia providers are often confronted with patients who fail to meet extubation parameters after surgery. These patients may experience difficulty weaning from mechanical ventilation and may require assistance with maintaining adequate tidal volumes. Diaphragm muscle fatigue is presently considered to be one of the causes of failure to wean from mechanical ventilation. \(^1\) It is estimated that 60% to 75% of the work of breathing (WOB) is performed by the diaphragm during normal respiration. \(^2\) The overall WOB consists of the following factors: (1) compliance work, the work required to overcome the elastic forces of the lung; (2) tissue-resistance work, the work required to overcome the viscosity of the lung and thoracic cage; and (3) airway resistance, the work required to overcome the resistance to the flow of air through the airways. \(^3\)

In the 1980s, pressure-support ventilation (PSV) was introduced as an assist mode to augment ventilation in select spontaneously breathing patients. \(^4,6\) Pressure-support ventilation decreases dyspnea and increases patient comfort by decreasing the resistance induced by the ventilator, the endotracheal tube, and secretions. \(^7,9\) When PSV is used, the patient’s spontaneous inspiration is augmented by delivering a preset pressure that is held constant throughout the inspiratory cycle. The patient controls the rate and timing of the delivered pressure, thus controlling flow and tidal volume \((V_T)\). Consequently, PSV decreases the overall WOB during weaning by supporting spontaneous inspiratory effort. \(^10,14\)

Sanders et al\(^{15}\) found that invasive technology such as endotracheal tubes and ventilator circuits increase the WOB. They suggested that the increase in WOB without the use of PSV may delay weaning from mechanical ventilation, thus increasing the chance for iatrogenic infections, increased length of stay, and subsequent rise in patient morbidity and healthcare costs. Sanders et al\(^{15}\) reported that the WOB decreased 38% to 64% with the application of 15 cm H\(_2\)O of PSV. Other studies have shown that PSV decreases respiratory rate, \(^10,16\) increases \(V_T\), \(^10,16\) reduces oxygen consumption, \(^9,11\) promotes recovery from diaphragm muscle fatigue, \(^1\) and allows the diaphragm to rest,
making weaning more comfortable and efficient.\textsuperscript{17-19}

Investigators have suggested that PSV lowers respiratory oxygen consumption by decreasing the WOB more than either synchronized intermittent mandatory ventilation\textsuperscript{5} or continuous positive airway pressure.\textsuperscript{6,20}

The latest mode of ventilation designed to augment the weaning process is called proportional assist ventilation \textsuperscript{5} or continuous positive airway pressure.\textsuperscript{6,20}

The purpose of this study was to examine the effects of PSV on diaphragm work by using a miniaturized ultrasonic transducer to directly measure diaphragm shortening. In addition, cardiopulmonary parameters associated with PSV were evaluated. This information will be useful for nurse anesthetists in understanding and using PSV to discontinue mechanical ventilation in surgery patients.

Materials and methods

A total of 15 Sprague-Dawley male rats were used for this study. The weight of rats ranged from 310 to 450 g with a mean weight of 400 g. The rats were maintained at a reversed 12-hour light-dark cycle, with lights on at 8:00 PM and off at 8:00 AM. This study was approved by the University of Kansas Medical Center Institutional Animal Use and Care (Kansas City, Kan).

The rats were anesthetized with sodium pentobarbital (65-80 mg/kg of body weight) administered via intraperitoneal injection. Atropine (0.10 mg/kg of body weight) was administered intraperitoneally to reduce respiratory secretions. When a surgical plane of anesthesia was reached, assessed by the pinch test and corneal reflex test, the following procedures were performed:

The trachea was exposed and cannulated using polyethylene 240 tubing. Next, a catheter (4F) was inserted in the oral cavity and advanced down the esophagus until the catheter tip was 1 to 2 cm above the diaphragm. The catheter was connected to a pressure transducer for continuous monitoring of esophageal pressure, which served as a measure of intrathoracic pressure (ITP).

A polyethylene (50) catheter was inserted into the left femoral artery and advanced until the catheter tip was in the descending aorta, approximately 1.5 cm below the renal arteries. The catheter was connected to a pressure transducer-recorder system for measuring systolic, diastolic, and mean arterial pressures (MAPs) and heart rate. This catheter also was used for measuring arterial blood gases, including pH, arterial partial pressure of carbon dioxide (PaCO\textsubscript{2}), arterial partial pressure of oxygen, bicarbonate, and oxygen saturation (blood sample volume was 100 µL). A thermocouple catheter was inserted in the left carotid artery and advanced until the catheter was positioned in the aortic arch and connected to a cardiac output monitor.

A second polyethylene (50) catheter was inserted in the right jugular vein and the tip advanced into the right atrium for measuring central venous pressure (CVP). In addition, this catheter was used as the site for injecting saline (0.5 mL) for determination of cardiac output (CO) using the thermal dilution technique. All catheter positions were verified by autopsy at the conclusion of the experiment.

The diaphragm was exposed via an abdominal midline incision. A miniaturized ultrasonic transducer for measuring diaphragm shortening was attached to the inferior surface of the middle costal portion of the right hemidiaphragm. The abdominal incision was not closed to allow assessment of sensor attachment during the experiment. The ultrasonic transducer was coupled to a Crystal Biotech Tracker (Crystal Biotech, Northborough, Mass). The instrument used conventional ultrasonic transmission-reflection principles to measure the distance between the transducer and a point of change in medium density within the diaphragm. The instrument was adjusted to track sound waves reflected from a reference plane 0.2 to 0.3 mm from the inferior thoracic diaphragm surface, providing a continuous, dynamic measurement of diaphragm thickness. It was assumed that the volume of the muscle cell does not change during contraction and relaxation. Therefore, during contraction, muscle cell diameter increased in direct proportion to decreased muscle cell length. Consequently, the increase in diaphragm thickness during inspiration is related directly to the overall extent of diaphragm shortening. Thus, during inspiration, the movement of the reference plane is directly proportional to the degree of diaphragm shortening. The extent to which the reference plane moved was designated as the percentage of fractional thickening (Figure 1). Earlier studies supported the miniaturized ultrasonic transducer as a device that measures diaphragm shortening with precision and accuracy during normoxia, hypoxia, and hypercapnia.\textsuperscript{13,23}

Once the animal preparation was completed, the
rat was connected to a Siemens Servo 300 ventilator set (Dräger Medical, Telford, Pa) as follows: PSV, 0 cm H2O; trigger sensitivity, 0; and end-expiratory pressure, 1 cm H2O. Pressure-support ventilation was increased sequentially by increments of 2 cm H2O every 2 minutes to 10 cm H2O and then sequentially returned to 0 cm H2O. Waveform measurements of arterial blood pressure, CVP, diaphragm shortening, ITP, end-tidal CO2 (PETCO2) and peak inspiratory pressure were obtained throughout the experiment via a CODAS computer data acquisition software package (DataQ Instruments, Inc, Akron, Ohio). Tidal volume and respiratory rate (f) were measured during the last 20 seconds of each 2-minute period. An analog signal from the Siemens ventilator to the computer was established to provide an accurate and precise continuous measure of VT. Cardiac output and arterial blood gases were measured following a 5-minute stabilization period at PSV 0 and 10 cm H2O.

Power analysis revealed that 15 animals would allow detection of an effect size of 0.15 with 80% power at a type I error rate of 5%. All measurements were compared using the 1-way repeated-measures analysis of variance and the Tukey procedure for post-hoc multiple comparisons of group means (SPSS-pc; SPSS, Inc., Chicago, Ill).

**Results**

Variables measured or calculated from the experiment included MAP, CVP, CO, systemic vascular resistance, peak inspiratory pressure, VT, f, minute ventilation (V̇E), PETCO2, ITP, and fractional thickening.

As shown in Figure 2, when PSV was increased from 0 to 10 cm H2O, a significant decrease in CO from 282 to 200 mL/min per kilogram occurred, F (1, 14) = 13, P = .0060. In addition, an increase in CVP from –0.90 cm H2O to approximately –0.01 cm H2O was observed, F (1, 14) = 5.75, P = .0310. Increasing PSV from 0 to 10 cm H2O resulted in an insignificant decrease in MAP, 107 to 98 mm Hg (P = .0740). Systemic vascular resistance increased 26%, which was not statistically significant (P = .0830).

Increasing PSV in increments of 2 cm H2O up to 10 cm H2O resulted in progressive decreases in respiratory rate (Figure 3). At a PSV of 10 cm H2O, the respiratory rate was statistically significantly different from baseline, F (1, 14) = 371.89, P = .0010. Minute ventilation increased significantly from 210 mL/min per kilogram at a PSV of 0 cm H2O to 400 mL/min per kilogram at a PSV of 10 cm H2O, F (1, 14) = 39.39, P = .0001. The V̇E increase accompanied by the decrease in respiratory rate associated with increasing PSV resulted in significant increases in V̇T from 2.7 mL at a PSV of 0 cm H2O to 6.7 mL at a PSV of 10 cm H2O, F (1,14) = 959.73, P < .0001. With the application of PSV, there was a decrease in PETCO2 (from 38 to 32 mm Hg); however, this decrease was not significant (P = .3300). End-inspiratory ITP became progressively less negative with each 2-cm H2O increase in PSV (Figure 4). At a PSV of 10 cm H2O, the end-inspiratory ITP was significantly different from baseline, F (1, 14) = 139.13, P < .0010. End-expiratory ITP remained unchanged with incremental increases in PSV. There were no significant changes in fractional thickening of the diaphragm among the PSV levels. At a PSV of 0 cm H2O PSV, fractional thickening was 24.38% and only increased to 26.63% at a PSV of 10 cm H2O, which was not statistically significant, F (1,14) = 2.57, P = .1300 (Figure 5). However, the unchanged diaphragm shortening occurred in the presence of progressive decreases in inspiratory ITP.

**Discussion**

An index of the work of the diaphragm (Wd) is the product of the difference between end-expiratory and end-

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**Figure 1.** Illustrates the placement of the ultrasonic sensor on the right hemidiaphragm in relation to the central tendon muscle

As the muscle contracts, the diaphragm becomes thicker and, thus, shortens, which causes the increase in the amplitude of the signal. On relaxation of the diaphragm, the muscle is not as thick and the signal returns to the baseline. During contraction of the muscle, the extent of the reference plane (f) movement is proportional to DS.

DS indicates diaphragm shortening; % FT, percentage of fractional thickening.
inspiratory ITP (ΔITP) times diaphragm shortening.

\[ W_D = \Delta ITP \times DS \]

By increasing PSV from 0 to 10 cm H_2O, the ΔITP (see Figure 4) was decreased by 33%. Consequently, because diaphragm shortening was unchanged with increasing PSV, there was an approximate 33% decrease in diaphragm work per breath. In addition, the decrease in the respiratory rate with increasing PSV resulted in a further decrease in the \( W_D \) per minute. Thus, the decrease in the \( W_D \) decreased the diaphragm oxygen consumption and protected the diaphragm muscle from fatigue, which would enhance weaning from mechanical ventilation. This supports the theory of MacIntyre\textsuperscript{24} and MacIntyre et al\textsuperscript{25} that PSV is an energy-efficient form of reducing the workload on the diaphragm.

Because PSV decreases the resistance from endotra-
Figure 4. Mean and SEM for intrathoracic pressure (ITP) at the end of expiration and end of inspiration at various levels of pressure-support ventilation (PSV)

The letter “d” after numbers indicates decreasing the amount of PSV.

Figure 5. Mean and SEM for fractional thickening of the diaphragm at different levels of pressure-support ventilation (PSV)

The letter “d” after numbers indicates decreasing the amount of PSV.
cheal tubes and ventilatory circuitry, diaphragm shortening should be enhanced with increasing PSV. When PSV levels increased, $V_T$ and $V_E$ increased, resulting in augmentation of alveolar ventilation and, thus, a reduction in $P_{aCO_2}$. The lower $P_{aCO_2}$ would decrease the activity of the central nervous system respiratory centers. If this resulted in a decrease in the duration of inspiration, the degree of activation of the diaphragm muscle would be reduced, and, thus, there would be less diaphragm shortening. Alternatively, the decrease in central nervous system respiratory center activity may diminish the frequency of phrenic nerve action potentials. Therefore, there would be a reduction in the magnitude of diaphragm activation. Either of these 2 mechanisms could account for the absence of an increase in diaphragm shortening with a decreasing load ($\Delta IT_P$). The possibility of decreased inspiratory duration and/or phrenic nerve discharge frequency is supported by the observations of Uchiyama et al,\textsuperscript{14} who found that peak diaphragm electromyogram signals were decreased with application of PSV.

During inspiration, the thorax is enlarged by a lowering of the diaphragm due to contraction of its muscle fibers and by elevation and expansion of the thorax (ribs and sternum).\textsuperscript{26} Consequently, the chest expands anteroposteriorly (coronal axis), transversely (horizontal axis), and vertically (median or cephalocaudal axis). The finding that an increased $V_T$ with PSV without a change in diaphragm shortening indicated that during inspiration there was an augmentation of chest movement in the coronal and horizontal axes.

A major hemodynamic effect associated with the application of PSV in this study was a 30% decrease in CO with a PSV of 10 cm H$_2$O. This finding supports the work of Dries et al\textsuperscript{27} in cardiac surgery patients in which they observed a decrease in CO with higher levels of PSV. Putensen et al,\textsuperscript{28} in examining the effects of spontaneous ventilation vs PSV on the ventilation-perfusion ratio, reported a significant decrease in CO at high levels of PSV. Dries et al\textsuperscript{27} found that as PSV was decreased, subsequent increases occurred in heart rate, MAP, and pulmonary capillary wedge pressure. Increasing ITP with application of PSV resulted in a decrease in right ventricular filling that caused CO to decrease. Consequently, PSV increased ITP, which impaired venous return and, hence, CO.

To summarize, PSV is a partial assist mode of ventilation that can be used by anesthesia providers to augment spontaneously breathing patients who may not meet extubation criteria following surgery. This mode of ventilation is more comfortable for the patient and improves patient-ventilator interaction.\textsuperscript{24,29} The results of this investigation demonstrated there was a decrease in $W_D$, although diaphragm shortening remained significantly unchanged with PSV. Thus, PSV, by decreasing diaphragm work, decreases diaphragm oxygen demand, which may prevent diaphragm fatigue, one of the main causes of failure to wean from mechanical ventilation.

Monitoring $V_E$, as a respiratory muscle load indicator,\textsuperscript{30} and monitoring saturation of arterial oxygen\textsuperscript{31,32} when weaning patients from mechanical ventilators are prudent clinical measures. By using PSV during weaning to decrease the imposed WOB caused by the endotracheal tube and circuitry, $V_T$ is improved while respiratory rate decreases, thus improving $V_E$. Furthermore, this study showed that the increase in $V_T$ and, thus, alveolar ventilation improved with the use of PSV resulting in decreased $PET_{CO_2}$.

Further study of PSV compared with other modes of ventilation (such as volume support) is essential for determining the most effective method for discontinuing patients from mechanical ventilation. Because new modes of mechanical ventilation are used in the clinical setting each year, anesthesia providers need to understand how the modes affect the respiratory muscles, in particular, the diaphragm, in order to provide optimal patient care.

REFERENCES


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