Diaphragmatic Contraction during Assisted Mechanical Ventilation*

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Indirect evidence from airway pressure recordings in mechanically ventilated patients suggests that the diaphragm exhibits contractile activity beyond that required to trigger a ventilator-assisted breath. We used the diaphragmatic EMG to provide direct evidence of persistent contractile activity and studied the effects of alterations in ventilator-delivered flow rate and tidal volume on the duration of diaphragmatic contraction. The duration of contraction was expressed in terms of inspired volume. During a single breath, diaphragmatic force generation ceases at the point of peak electromyographic activity; hence, the inspired volume at peak EMG is the volume at the diaphragmatic off-switch (Voff). Ventilator-delivered flow rate and tidal volume were varied during assisted (patient-initiated) and controlled (ventilator-initiated) breaths while diaphragmatic EMG and inspired volume were recorded simultaneously in ten patients with a variety of illnesses requiring mechanical ventilation. Spontaneous ventilator-unassisted breaths were also recorded for comparison. We found that (1) during assisted breaths, diaphragmatic activity continued after the ventilator was triggered, (2) Voff was usually close to spontaneous tidal volume, (3) Voff increased significantly as ventilator-delivered flow rate increased, and (4) controlled breaths may also be associated with phasic electromyographic activity. The data have implications for resting patients on assisted ventilation. (Chest 1989; 96:130-35)

Recent data indicate that during assisted mechanical ventilation the diaphragm continues to contract after triggering the ventilator, dispelling the commonly held belief that diaphragmatic muscle contraction ceases after the machine is triggered. Variations in airway pressure and measurements of the mechanical work of breathing have been cited by some authors as evidence of continued inspiratory muscle contraction.

Ayres et al. showed that patients with COPD who were ventilated with intermittent positive-pressure breathing have lower airway pressures during assisted breaths than during controlled unassisted breaths of the same tidal volume. The same observation has been made in normal humans and in animals.

Marini and associates demonstrated that patients with pulmonary disease may perform significant amounts of muscle work during assisted mechanical ventilation. These data provide strong indirect evidence for continued diaphragmatic contraction beyond triggering the ventilator; however, the duration of this contraction and the factors influencing the duration of inspiratory muscle contraction have not been well characterized during mechanical ventilation in humans with illness.

The duration of diaphragmatic contraction can be accurately determined by examination of the diaphragmatic EMG. Evidence indicates that inspiration is terminated and diaphragmatic contraction turned off in response to volume-related stretch receptor feedback. For this reason, and in order to study the effects of delivered flow rate (volume/time), we chose to express contraction duration in terms of inspired volume. Contraction duration, therefore, is characterized by the inspired volume at peak electromyographic activity and is referred to as the volume at diaphragmatic off-switch (Voff). This investigation was undertaken to confirm that persistent diaphragmatic contraction occurs during ventilator-assisted breaths in patients with pulmonary disease and, further, to determine if alterations in ventilator-delivered tidal volume or flow rate affect the duration of diaphragmatic contraction.

Materials and Methods

Ten intubated patients receiving mechanical ventilation were studied (Tables 1 and 2). At the time of study, the patients were clinically stable, capable of some spontaneous ventilation, and without positive end-expiratory pressure. The patients were judged ready for weaning from the ventilator by their attending physicians, and mechanical ventilation was discontinued shortly after the study except in patients 1 and 7. These two patients had evidence of paradoxical abdominal motion during spontaneous breathing and therefore may have had diaphragmatic fatigue.

Airway pressure, inspiratory flow rate, diaphragmatic EMG, and inspiratory volume were measured during each experiment. The diaphragmatic EMG was recorded from two silver/silver chloride adhesive cutaneous leads placed in each nipple line at the costal arch with a common lead in the right axillary line at the tenth rib. The electromyographic signal was processed through a differential isolation amplifier and was bandpass filtered between 30 and 500 Hz. Electrocardiographic interference was reduced using a gating device similar to one described by Prechyl et al. Airflow was measured by a pneumotachograph (Fleisch No. 3) and differential

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pressure transducer (Validyne MP45) in the inspiratory limb of the ventilator circuit near the endotracheal tube. Flow was electronically integrated to provide inspired tidal volume. The signals were amplified, displayed, and recorded on an oscillographic recorder for later analysis (Electronics for Medicine VR6).

The study protocol began with a period of spontaneous breathing followed by ventilator-delivered/assist/control breaths and then ventilator-controlled breaths. Ventilator-delivered inspiratory tidal volume and flow rate were varied in multiples of the observed spontaneous values during the assisted and controlled breath portion of the study. Patients initiated assisted breaths by developing a small negative airway pressure, which was followed by ventilator-assisted inspiration at the selected flow rate and tidal volume. Controlled breaths were similar to the assisted breaths but initiated by the ventilator. Spontaneous breaths were drawn through the ventilator but not assisted. The sensitivity of the demand valve was 0.5 cm H₂O for both assisted and spontaneous breaths.

A calibrated volume ventilator (Puritan-Bennett 7200) was used to perform the experiment. Patients were observed for one hour on settings previously chosen by their attending physicians. The subjects were then allowed to breathe spontaneously (without assistance) through the ventilator for a target period of five minutes. Tidal volume, inspiratory flow rate, and diaphragmatic EMG were recorded simultaneously for five to seven sequential spontaneous breaths at the end of the five-minute period. Patients 1 and 7 were unable to breathe spontaneously for this length of time, so data were recorded after only two to three minutes of spontaneous breathing. Subjects then rested for ten minutes on their original ventilator settings. Five to seven assisted breaths at nine combinations of tidal volume and flow rate derived from the measured values during spontaneous breathing were delivered in random order. Tidal volumes of 1, 1.5, 2, and 2.5 times the patient's spontaneous tidal volume and flow rates of 0.5, 1, 1.5, 2, and 2.5 times the spontaneous flow rate were used. Only nine tidal volume-flow rate combinations (of the 20 possible) were attempted with each patient, in order to reduce the possibility of fatigue. Combinations with high tidal volume and low flow rate were frequently omitted, as they interfered with adequate inspiratory time. After another ten-minute rest, controlled breaths were delivered at the same tidal volume-flow rate combinations.

For each tidal volume-flow rate combination recorded, the last three breaths showing a clear electromyographic peak, ie unobscured by ECG, were selected for analysis. For each breath the inspiratory volume at the peak of electromyographic activity was determined by direct inspection of the raw recordings of diaphragmatic EMG and tidal volume. The inspiratory volumes at the peak of electromyographic activity for the three breaths were then averaged to obtain the Voff at a particular tidal volume-flow rate combination. Voff was expressed as a fraction of the measured spontaneous tidal volume, as were the delivered tidal volumes and flow rates, in order to facilitate interpatient comparison. The Voff values for all of the patients were plotted against ventilator-delivered flow rate at isovolume; flow rates for an individual patient at the same tidal volume were related by a line through the points (Fig 1A). The Voff was plotted similarly against ventilator-delivered tidal volume at isoflow (Fig 1B). Regression equations and the slope of the regression line were determined for each Voff vs flow rate (isovolume) and Voff vs tidal volume (isoflow) relation. The mean Voff for the entire group was determined using the Voff at all settings, for all patients.

Two approaches were used to decide if there was an effect of delivered flow rate or tidal volume on the Voff. Data were grouped by flow rate and then by tidal volume. First, for all patients, regardless of delivered volume, Voff values at the lowest flow rates (≤1.0 times spontaneous) were compared to Voff values at highest flows (≥2.0 times spontaneous). Similarly, for all patients, regardless of delivered flow, Voff values at lowest delivered tidal volumes were compared to Voff values at highest volumes. Second, the mean slope of all of the Voff vs tidal volume and then Voff vs flow rate regressions were tested for significant difference from zero using Student's t-test; a significant difference (p<0.05) supported an effect of flow rate or tidal volume on Voff.

RESULTS

Diaphragmatic EMG persisted after the ventilator was triggered for assisted breaths despite alterations in flow rate and tidal volume (Fig 2). The mean Voff for the entire group during assisted breaths at all ventilator settings was 93±34 (SD) percent of the spontaneous tidal volume, with a range of 25 to 195 percent. Comparison of Voff at low flow rates to that at high flow rates demonstrates that alterations in delivered flow rate significantly affected Voff (p=0.0024). This was confirmed by examining the Voff vs flow rate regression line slopes (p<0.00001). An effect of delivered tidal volume on Voff was not clearly demonstrated (p=0.71 for low tidal volume vs high tidal volume comparison; p=0.017 for slope comparison).

During controlled breaths, there was no phasic diaphragmatic electromyographic activity until the ventilator-delivered tidal volume was close to the patient's spontaneous tidal volume (Fig 3). Electro-
myographic activity and a reduced peak inspiratory pressure were seen late in inspiration at lower tidal volumes, indicating some diaphragmatic activity during these ventilator-initiated breaths.

The lowest Voff values were in two patients with suspected diaphragmatic fatigue (mean, 58 ± 29 percent of spontaneous tidal volume); this was significantly different from the mean Voff of the entire group.
We found that diaphragmatic contractile activity ceased during ventilator-assisted breaths at a volume close to each patient's measured spontaneous tidal volume, except in two patients with possible diaphragmatic fatigue. In these two patients, Voff was consistently less than spontaneous tidal volume. Increasing ventilator-delivered inspiratory flow rate led to increases in Voff; however, a clear statement about the effect of delivered tidal volume on Voff cannot be made. During controlled breaths initiated by the ventilator, there is no electromyographic activity present except when the delivered tidal volume approaches the patient's spontaneous tidal volume. At low tidal volumes, controlled breaths are assisted late in the breath. The pressure waveform often appears similar in contour to other controlled breaths, but the peak pressure is lower.

A current model for control of phasic breathing has been constructed primarily from observations in animals and suggests that increasing flow rate should affect Voff. In its simplest form (refer to Fig 4), the model proposes a central threshold for inspiratory off-switch. The central off-switch interacts with stretch receptor volume information transmitted by the vagi to determine the volume of inspiratory termination. Threshold for off-switch decreases with time after the onset of inspiration; a region of graded inhibition follows the off-switch threshold and produces a snowball effect, with some inhibition allowing greater inhibition until inspiration terminates. Inspiratory flow rate appears to feed back as well, probably at a submedullary level, resulting in reflex changes in

DISCUSSION

This study provides direct electromyographic evidence of persistent diaphragmatic contractile activity in patients with a variety of diseases requiring mechanical ventilation in the assist/control mode. Persistent diaphragmatic contraction during ventilator-assisted breaths has been indirectly demonstrated in normal animals and humans by measuring airway pressure and in ill humans by measuring the mechanical work of breathing. Inspection of the diaphragmatic EMG allows precise determination of contraction duration thus facilitating the study of tidal volume and flow rate alteration on the contraction's duration. We chose to express the duration of electromyographic activity in terms of inspired tidal volume because available evidence suggests that volume feedback from stretch receptors, in part, controls inspiratory duration.

We found that diaphragmatic contractile activity ceased during ventilator-assisted breaths at a volume.
phrenic output and diaphragmatic EMG. The model posits a higher off-switch volume with increasing flow rates, since volume feedback would intersect the off-switch threshold prior to significant decrease. Our results provide human data to support this model.

Since the Hering-Breuer reflex is variably active in humans, ventilator-delivered tidal volume variation could affect Voff in some individuals. Tidal volume delivered during one breath would affect the subsequent breath, altering Voff. Our analysis relies heavily on meaned data, reducing the chance of showing a statistically significant effect of tidal volume (or flow rate) on Voff. Because of this, although we were unable to demonstrate it, the possibility of delivered tidal volume affecting Voff still exists. A combined effect of tidal volume and flow rate variation greater than their individual effects may exist as well. A larger number of patients would be necessary to address these issues.

We noted variability in the Voff both within and between patients. This variability may be attributable in part to the central respiratory drive's response to stimuli such as stretch receptor input related to pulmonary mechanical properties, body temperature, and cortical and chemoreceptor input. An effect on Voff from both elastic and resistive loading has been suggested in animals: the vagal influence on medullary control of inspiratory off-switch has been shown to be greater in restrictive than in obstructive disease. The peak inspiratory electromyographic activity precedes maximal volume during spontaneous breathing; the amount of this lag has not been determined in humans but is around 200 to 300 ms in cats and increases with increasing airway resistance. Cortical input may be reduced by random sequencing of tidal volume and flow rate changes; our patients were acclimated to the ventilator, relaxed, and accustomed to changes in their ventilator settings. Variability in the Voff response to ventilator inflations between patients is, therefore, not unexpected. Inpatient differences in Voff were reduced by expressing Voff as a fraction of spontaneous tidal volume.

Since diaphragmatic electromyographic activity indicates diaphragmatic contractile activity and tension development during assisted breaths, certainly metabolic "work," and probably mechanical work, is being performed. Marini et al demonstrated that ventilator-determined inspiratory flow rate significantly influences a patient's mechanical work performed during assist-control ventilation, with increasing flow rates decreasing inspiratory work. Our data also suggest that even high flow rates may not completely rest the respiratory muscles during assist-control ventilation. In addition, diaphragmatic contraction and performance of work may be seen with controlled ventilation at inappropriate tidal volumes and flow rates. Because the ventilator performs all of the inspiratory work of breathing after Voff, the quantity of mechanical work performed during assisted ventilation is likely dependent on tidal volume as a portion of the total minute ventilation as well as ventilator-delivered flow rate. At low flow rate and tidal volume settings, the diaphragm may contract against a ventilator-imposed inspiratory load, increasing inspiratory work. The diaphragm should be rested more effectively during controlled ventilation than with assist-control, as there is no electromyographic activity during controlled ventilation as long as delivered tidal volume and flow rate are above the patient's spontaneous tidal volume and flow rate. Alternatively, diaphragmatic contraction beyond triggering the ventilator may be beneficial and facilitate weaning from mechanical ventilation. Neurumuscular control loop integrity would be maintained, perhaps forestalling muscle atrophy and asynchronous breathing described in patients ventilated for prolonged periods.

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