Phrenic Nerve and Vagal Nerve activities during Differential Lung Ventilation in Cats

Toshiharu KASABA and Yoshihiro KOSAKA

The effect of differential lung ventilation (DLV) on afferent vagal and efferent phrenic nerve activities was studied in urethane anesthetized cats. One endotracheal tube was inserted into the left bronchus to ventilate its side lung. Another tube was inserted until its tip reached about 1 cm above the carina to ventilate the right lung. Using two respirators, each lung was ventilated independently. Using hooked silver electrodes, the vagal and phrenic nerve activities were recorded.

The afferent vagal nerve was activated in concurrence with lung inflation at any ventilation rate. The right and left vagal nerves were activated by right and left lung ventilation, respectively. On the other hand, the right and left efferent phrenic nerves were synchronized, whether the ventilation was disused or ventilation was achieved by right or left one lung ventilation or even by asynchronous DLV.

The phrenic nerve activity was surpressed by one-lung, right or left, ventilation independently, so that the rhythm of the phrenic nerve was disturbed by asynchronous DLV. From these results, to reduce the stress of patients during asychronous DLV, it was considered that patients need heavier sedation than a usual mechanical ventilatory support. (Key words: differential lung ventilation, phrenic nerve activity, vagal nerve activity)

(Kasaba T, Kosaka Y: Phrenic nerve and vagal nerve activities during differential lung ventilation in cats. J Anesth 2: 170–175, 1988)

Differential lung ventilation (DLV) is an effective mode of mechanical ventilatory support for patients with unilateral lung disease and the operative care of pulmonary surgery patients[1–7]. Synchronous DLV is accomplished usually by synchronizing two ventilators using an external electric equipment[1–4]. On the other hand, the asynchronous DLV system has been introduced as being less complex and easier to use than two synchronized ventilators. Besides, data reported on circulation during asynchronous DLV suggest no need to synchronize ventilators[5–7].

However, asynchronous DLV produces non-physiological ventilation that is to say, one lung is in an inspiratory phase, while the other is in an expiratory phase. Functional disturbance of the respiratory regulation system may be anticipated during asynchronous DLV.

The aim of the present study is to obtain information on ventilator interference with respirator control mechanisms, and to evaluate the phrenic and vagal nerve activities during asynchronous DLV. In this study we first examined the effect of DLV on the right and left afferent vagal nerve activities, and then the right and left efferent phrenic nerve activities during asynchronous DLV.

Department of Anesthesiology, Shimane Medical University, Izumo, Japan

Address reprint requests to Dr. Kasaba: Department of Anesthesiology, Shimane Medical University, 89-1 Enya-cho, Izumo, 693 Japan

Material and Methods

Preparation

Eight adult cats weighing 2.5–3.8 kg were used. General anesthesia was induced with halothane and maintained with urethane (1 g/kg). After endotracheal intubation (6 mm, I.D.), they were paralysed with pancuronium bromide (0.2 mg/kg) and mechanically ventilated with a respirator (Shinano, SN-480-5). The femoral vein was cannulated for infusion and drug administration. The femoral artery was cannulated for blood sampling and for monitoring the blood pressure. The chest wall was opened around the sixth rib, and utmost care was taken to unhurt the vagal nerve. After extubating the preintubated endotracheal tube, one endotracheal tube (3 mm, I.D.) was inserted into the left bronchus and was ligated around the bronchus to prevent leakage around the tube. Another tube (3 mm, I.D.) was inserted until its tip reached about 1 cm above the carina to ventilate the right lung and was ligated around the trachea. Using two respirators, each lung was ventilated independently. Simultaneous ventilation of both the right and left lungs was achieved by means of one respirator using a Y connector. The respiratory rate was adjusted to synchronize with phrenic nerve discharge. The tidal volume of the respirator was controlled by the value of Pa_{CO_2} to remain within a normal range (35 $\sim$ 45 mmHg). Both the right and left lungs were ventilated simultaneously with a tidal volume of 30 $\sim$ 40 ml, and in DLV, each lung was ventilated with a half of the tidal volume independently. The chest movement was monitored pneumographically using resistance strain gages. The blood pressure was continuously monitored using sphygmomanometer. Intermittent arterial blood gas analysis for Pa_{O_2}, Pa_{CO_2} and pH was performed using a Radiometer ABL2 blood-gas analyser. Oxygen was added to the inspired gas to maintain Pa_{O_2} higher than 100 mmHg.

Recording

Access to the phrenic and vagal nerves was achieved by a medial frontal incision in the neck. The right and left vagal nerves were separated from the common carotid artery, and were dissected from the covering sheaths. The right and left phrenic nerves were found where they bent off caudally from their cervical roots. The nerves were dissected from connective tissue, the outer isolating sheaths were removed and the nerves were cut in their lower extrathoratic portions. The phrenic and vagal nerve activities were recorded using silver hook electrodes. These nerves and electrodes were immersed in paraffin solution.

A signal from the recording electrode was passed through a preamplifier (Nihonkoden, S 1516) and amplifier (Nihonkoden, AVH-10) before it was displayed on an osciloscope (Nihonkoden, VC-9). In addition, for discrimination between the phrenic nerve activity and the pneumogram, the phrenic nerve was rectified and integrated (Nihonkoden, EI-601-G). All data were recorded with a photo-recorder or jet ink-recorder and stored in a data-recorder (Sony, DFR-3415).

Analysis

The continuity of the afferent vagal nerve activity from pulmonary stretch receptors to the respiratory center was confirmed to synchronize with lung inflation. The right and left lungs were ventilated simultaneously or independently and the right and left vagal nerve activities were recorded simultaneously. To further investigate of the role of afferent vagal nerve, the nerve was resected and ventilation was carried out at different ventilation rates. Whether the right and left efferent phrenic nerves were synchronized or not, both the right and left phrenic nerve activities were recorded simultaneously in different ventilatory patterns, namely, disuse of a ventilator, right or left one lung ventilation and asynchronous DLV. To determine the effect of DLV, the efferent phrenic nerve activity was recorded with a pneumograph. Asynchronous ventilation was performed using two ventilators by ventilating each lung independently at a different rate.

Results

1) Afferent vagal nerve activity during

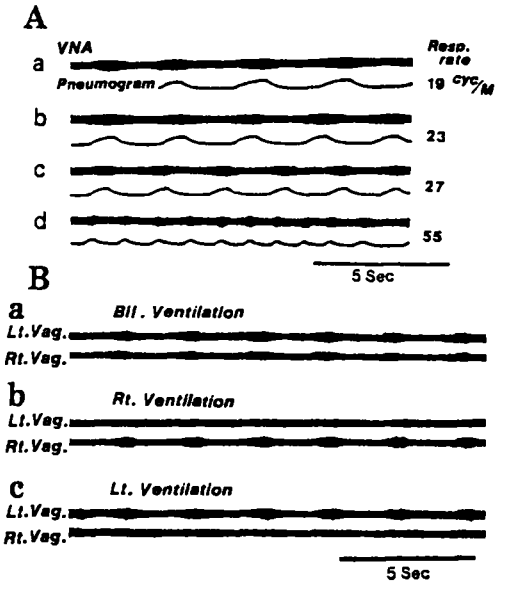

Fig. 1.

A: Afferent vagal nerve activities during bilateral lung ventilation at rates ranging from 19 to 55 cycles/min (a ~ d). Vagal nerve was activated in concurrence with lung inflation at any ventilation rate.

B: Right and left vagal nerve activities. Vagal nerve activities were recorded simultaneouly during (a) bilateral lung ventilation, (b) right lung ventilation and (c) left lung ventilation at a respiratory rate of 23 cycle/min. Vagal nerve was activated only at the site of lung ventilation. VNA: Vagal nerve activity. Lt.Vag.: Left vagal nerve activity. Rt.Vag.: Right vagal nerve activity.

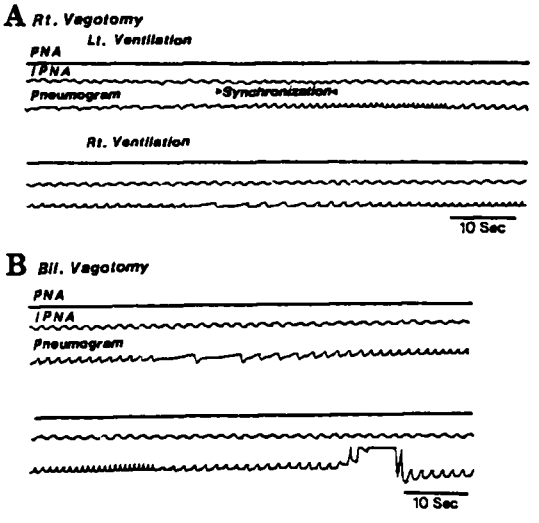

Fig. 2. Effects of vagotomy on phrenic nerve activity.

A: After resection of right vagal nerve in its upper portion. Efferent phrenic nerve discharge was synchronized at rates ranging from 30 to 40 cycles/min (upper trace) only by left lung ventilation and no change was seen by right lung ventilation at rates rangeing from 12 to 60 cycles/min.

B: Bilateral vagotomy resulted in disappearance of afferent input. Efferent phrenic nerve discharge stayed almost constant by either lung ventilation or PEEP (upper and lower traces are continued).

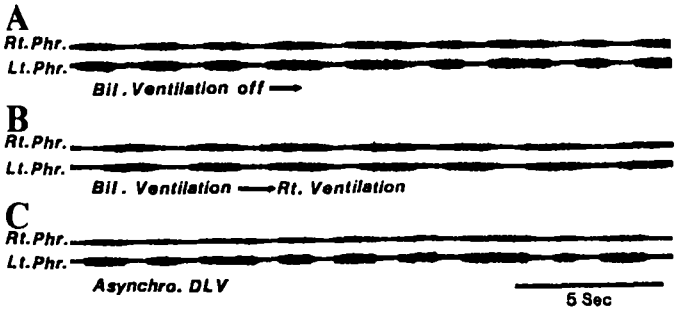

Fig. 3. Right and left phrenic nerve activities were recorded simultaneously.

A: During bilateral ventilation and after discontinuation of ventilation. B: From bilateral ventilation to right ventilation. C: During asynchronized DLV. In these cases right and left phrenic nerve activities were synchronized each other. Rt.phr.: Right phrenic nerve activity. Lt.phr.: Left phrenic nerve activity. Asynchro. DLV: Asynchronous differential lung ventilation.

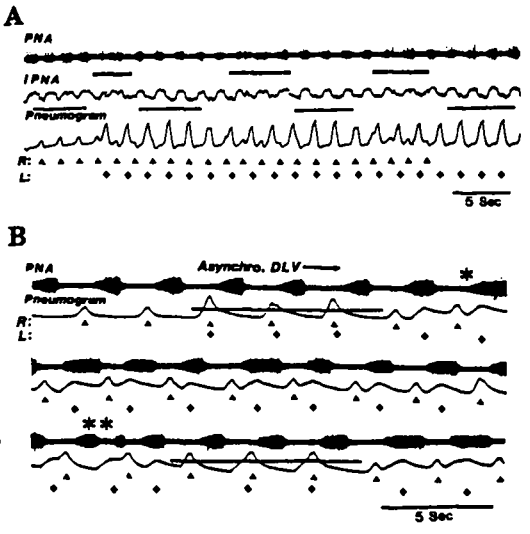

Fig. 4. Efferent phrenic nerve activity during DLV.

A: Right lung was ventilated at a rate of 35 cycles/min. Solid triangles indicate right lung ventilation. Left lung was ventilated at 30 cycles/min. Solid rhombi indicate left lung ventilation. Phrenic nerve activity was synchronized with right one lung ventilation (left side) and left one lung ventilation (right side). When right and left lung ventilation were set nearly in phase, phrenic nerve was activated regularly. When right and left lungs were ventilated out of phase, phrenic nerve was disturbed (broken line).

B: Right lung was ventilated at a rate of 22 cycles/min and left lung ventilation was performed at rates of 15 and 30 cycles/min. Solid triangles and rhombi indicate respective results. When left lung ventilation was set neary in phase to right ventilation, phrenic nerve was activated regularly (solid line). However, when left lung ventilation phase was shifted more from right lung ventilation, phrenic nerve discharge was prolonged (*) or shortened (**), depending on asynchronous ventilation. PNA: Phrenic nerve activity. IPNA: Integrated phrenic nerve activity. R: Right lung ventilation. L: Left lung ventilation.

DLV

The afferent vagal nerve was activated by lung ventilation. The activity was completely synchronized with the pneumogram at any ventilation rate (fig. 1A). The vagal nerve activities during DLV are shown in figure 1B. The right and left vagal nerves were activated by bilateral lung ventilation (fig. 1B-a), by right lung ventilation (fig. 1B-b), by left lung ventilation (fig. 1B-c). These results indicate that the vagal nerve was activated only when ipsilateral lung was inflated. To determine the effect of afferent input transmitted only through the ventilation site, vagotomy was performed (fig. 2). When the right vagus was resected (fig. 2A), the phrenic nerve was synchronized at some ventilatory rate (30 $\sim$ 40 breach per minute b.p.m.) by left lung ventilation. However, by right lung ventilation, the phrenic nerve was activated spontaneously and not influenced by lung ventilation. Bilateral vagotomy produced no such effects (fig. 2B).

2) Efferent phrenic nerve activity during DLV

The right and left phrenic nerve activities are shown in figure 3. Inspite of the respiratory changes, namely, disconnection of the respirator (fig. 3A), right lung ventilation (fig. 3B), or asynchronous DLV (fig. 3C), the right and left phrenic nerve discharges were synchronized with each other. These show synchronization of the efferent phrenic nerve discharge, regardress of the patterns of ventilation. The effect of asynchronous DLV on the phrenic nerve activity was studied (fig. 4). The rates of the both respirators were fixed at first (fig. 4A). The rate of one respirator was fixed and that of the other varied (fig. 4B). Independent ventilation of the right and left lungs resulted in regular activation of the phrenic nerve, if right and left ventilation were set almost in phase. However, when right and left lung ventilations were set out of phase, the phrenic nerve discharge was disturbed by lung ventilation.

Discussion

Patients with severe asymmetrical unilateral lung desease have been treated by DLV and unilateral PEEP when adequate gas exchange could not be maintained with standard mechanical ventilation[1–7]. East et al.[5] and others[6,7] have denied the need of synchronizing two ventilators when using

DLV with unilateral PEEP in gas exchange or control of hemodynamics. With regard to the respiratory rhythm, it is important to synchronyze patients' ventilation rhythm with artificial ventilation. Because if the patients' respiratory rhythm dose not synchronize with the respirator rhythm, they may be exposed to stress. The aim of the present investigation was to ascertain how different type of ventilation act upon the afferent activity in the vagal nerve and to examine the relation between this activity and the efferent phrenic nerve activity during DLV. In studies of the regulation of respiration, the phrenic nerve activity has been used as an indicator of central inspiratory activity and the vagal nerve activity has been used as an afferent input from pulmonary stretch receptors. Inflation of the lungs inhibits inspiration and collapse of the lungs stimulates it. By means of these vagus-mediated influences, the mechanical events of pulmonary inflation and collapse are linked to the central, neurochemical processes of respiratory control, providing one component in the self-regulation of respiration. When delivering DLV, the afferent vagal nerve was activated only at the infulated lung site. The role of vagus was confirmed by cutting the vagal nerve. This means that the afferent input enters from right or left pulmonary stretch receptors to the respiratory center independently. That is to say, the right vagal afferent input influences only right side lung ventilation. Synchronization with lung ventilation in a certain range by means of vagal nerve mediated input disappeared by vagotomy.

The efferent phrenic nerve activity, as an output of respiration, was synchronized whether the respirator was disconnected, or respiration was achieved by right lung ventilation or even right and left asynchronous DLV. This means that the phrenic nerve activity was synchronized even by any afferent vagal input. It has been reported that in application of usual bilateral ventilation, the afferent input produced by PEEP and HFPPV through the vagal nerve suppresses the phrenic nerve activity[8,9]. Lung inflation inhibits the inspiratory motor activity in anesthetized animals. This response is mediated by the Hering-Breuer lung inflation reflex which is excited by pulmonaly stretch receptors. Von Euler has described that the respiratory rhythm was produced at the brain stem and modulated by the afferent input from pulmonary stretch receptors[10]. An afferent input has an effect to change the rhythm of respiration. Vagal fibers from pulmonary stretch receptors penetrate the medulla, reach the solitary tract, and from there undergo medullary and pontine reticular formation[11]. From these findings, it is considered that a change in the respiratory rhythm occurs at the brain stem, and the output of rhythm of synchronization projects to phrenic motoneuron and synchronizes respiratory movement. Only right or left one lung ventilation is considered similar to usual ventilation in its effect on the rhythm of phyrenic nerve discharge. Ventilation of one lung with IPPV and the other with PEEP may not produce so much problem in regulation between the phrenic nerve activity and IPPV rhythm, because PEEP itself surpresses the phrenic nerve discharge and is not so concerned with respiratory rhythm. The rhythm in one lung IPPV is an important afferent input to generate respiratory rhythm. However, in asynchronous DLV, each lung IPPV is influenced independently, and as a results, the efferent phrenic nerves are disturbed by the afferent asynchronous input. The vagus trunk carries fibers which influence breath, because at least four sets of these nerve fibers are capable of powerfully affecting respiration[12]; these fibers being (1) fibers that mediate the Hering-Breuer reflex, (2) those repredenting the sensory innervation, which cause coughing or at least active expiration, (3) afferent fibers from baroreceptors in the arch of the aorta, which when stimulated, cause inhibition of breathing and fall in blood pressure, and (4) afferent fibers from the aortic bodies, which when stimulated, cause hyperpnea and elevation of blood pressure. We comfirmed that the cats had no hypotension (BP>80 mmHg), hypertention (BP<150 mmHg) nor hypoxia (Pa_{O_2}>100 mmHg)[13]. It was re-

ported that DLV and PEEP themselves do not change Pa_{CO_2} and our results agree with these finding. Therefore, except when the respirator is discused and the ventilation rate is changed, the influence of afferent fibers from baroreceptor and aortic bodies can be ignored. The carina at the bifurcation of the trachea is especially sensitive. So when delivering DLV, the effect of sensory innervation is also important.

These problems are often overcome by pharmacological interference with respiratory control mechanisms, which then introduces an adverse effects on sedation and muscle relaxation. From a neurophysiological point of view it would, therefore, be preferable if a ventilator could be physiologically adapted to patients. Though the action of non-physiological respiration to human being is not clear, it was considered that patients during asynchronous DLV need heavier sedation than an ordinary mechanical ventiatory support.

(Received Apr. 14, 1988, accepted for publication Jun. 11, 1988)

References

1. Gallagher TJ, Banner MJ, Smith RA: A simplified method of independent lung ventilation. Crit Care Med 8:396–399, 1980
2. Carlon GC, Ray C, Klein R, Goldiner PL, Miodownik S: Criteria for selective positive end-expiratory pressure and independent synchronized ventilation of each lung. Chest 74:501–507, 1978
3. Baehrendtz S, Hedenstierna G: Differential ventilation and selective positive end-expiratory pressure: Effects on patients with acute bilateral lung disease. Anesthesiology 61:511–517, 1984
4. Popovich Jr J, Sanders Jr OJ, Vij D, Polanski JJ, Conway WA: Differential lung ventilation with a modified ventilator. Crit Care Med 9:490–493, 1981
5. East TD, Pace NL, Westenskow DR: Synchronous versus asynchronous differential lung ventilation with PEEP after unilateral acid aspiration in the dog. Crit Care Med 11:441–444, 1983
6. Hillman KM, Barber JD: Asynchronous independent lung ventilation (AILV). Crit Care Med 8:390–395, 1980
7. Muneyuki M, Konishi K, Horiguchi R, Tsujimoto S, Saito M, Sakakura S, Konoshi A; Effects of alternating lung ventilation on cardiopulmonary function in dog. Anesthesiology 58:353–356, 1983
8. Jonzon A: Phrenic and vagal nerve activities during spontaneous respiration and positive-pressure ventilation. Acta Anaesthesiol Scand Suppl 64:29–35, 1977
9. Norsted T, Jonzon A, Rondio Z, Sedin G: Inhibition of phrenic nerve activity during positive-pressure ventilation at high and low frequencies. Acta Anaesthesiol Scand 30:521–528, 1986
10. Euler CV: On the central pattern generator for the basic breathing rhythmicity. J Appl Physiol Respirat Environ Exercise Physiol 55:1647–1659, 1983
11. Cohen MJ: Neurogenesis of respiratory rhythm in the mammal. Physiological Review 59:1105–1173, 1979
12. Lambertsen CJ: Neural control of respiration. Edited by Mountcastel. VB The C.V. Mosby Company, 1980, pp.1749–1773
13. Grundy EM, Chekrabarti MK, Whitwam JG: Efferent phrenic nerve activity during induced changes in arterial pressure. Br J Anaesth 58:1414–1421, 1986